DYSLIPIDEMIA IN CHRONIC KIDNEY DISEASE

CORRELATION TO STAGES OF CHRONIC KIDNEY

DISEASE - AN EVALUATION

DISSERATION SUBMITTED
FOR
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CERTIFICATE

This is to certify that this dissertation entitled **"DYSLIPIDEMIA IN CHRONIC KIDNEY DISEASE – CORRELATION TO STAGES OF CHRONIC KIDNEY DISEASE - AN EVALUATION"** is a bonafide record of work done by **Dr. SHAFIQUE.A** under my guidance and supervision in Tirunelveli Medical College Hospital during the period of his Post Graduate Study for M.D. (General Medicine) from 2007 – 2010.

Dr.M.R.Vairamuthuraju M.D.,
Additional Professor of Medicine
Department of Medicine
Tirunelveli Medical College Hospital
Tirunelveli.

Dr.J. Kaniraj Peter M.D.,
Professor and Head of the Department
Department of Medicine
Tirunelveli Medical College Hospital
Tirunelveli.

The Dean
Tirunelveli Medical College
Tirunelveli.

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INTRODUCTION

Cardiovascular disease is a major cause of mortality in patients with mild to moderate kidney disease and end stage renal disease[ESRD]. The principal reason to evaluate dyslipidemias in patients with chronic kidney disease is to detect abnormalities that may be treated to reduce the incidence of cardiovascular disease.

Since chronic Kidney disease is a progressive disease, the various lipid abnormalities vary from CKD stages 1- 5 . So it is prudent to look into various lipid abnormalities attributed to each stages of kidney disease.

In our hospital, there are many patients admitted last year fulfilling the criteria for chronic kidney disease and treated as inpatient or outpatient.

At present the medical treatment for kidney disease is improving and patients long term survival is improving. Peritoneal dialysis, hemodialysis and transplantation have revolutioned the prognosis of chronic kidney disease in recent time.

Although there is still controversy whether CKD represents an independent risk factor for incident cardiovascular disease, accumulating evidence over the last decade marks out cardiovascular disease as major cause of mortality in patients with mild to moderate CKD or ESRD.

Dyslipidemia has been established as a well known traditional risk factor for cardiovascular disease in the General Population and large scale observational studies have shown that patients with impaired renal function exhibit significant alterations in lipoprotein metabolism , which in their most advanced form may result in the development of severe Dyslipidemia.

The Study mainly focuses on the lipid abnormalities attributed to different stages of chronic kidney disease.

AIM OF THE STUDY

1. To analyze the lipid abnormalities in Patients with **Non Diabetic Chronic Kidney Disease.**
2. To find the correlation in various stages of Chronic Kidney disease with Lipid abnormalities.
3. To find which lipid abnormalities is more common in the study group.

Inclusion criteria for case selection :

- All newly detected Non diabetic Chronic kidney disease from Sep 2008 to Sep 2009.
- Age Group 15-65yrs.
- Elevated Renal Parameters with Urea : Creatinine ratio <20 .
- Stable creatinine values taken 4 days apart with variation less than 20 %.
- Ultrasonographic evidence of Chronic Kidney Disease with kidney size less or equal to 9cm .
- Normal Values of LDL< 100mg/dl,HDL <40 [M]<50[F]mg/dl, T. Chol<200mg/dl,TGL-150 mg/dl has been taken cut- off range for this study.

Exclusion criteria for the case selection :

1. Patients with known h/o diabetes mellitus and patients with Diabetic kidney disease , with elevated random blood sugar values of >200mg% were excluded.
2. Ischemic heart disease on treatment already were excluded.
3. Severe Comorbid conditions like pneumonia, alcoholic Liver disease and hypotension .
4. Those who are taking Beta blocker and thiazide diuretics at time of study were excluded.
5. Patients with H/o intake of anti cholestrelomic agents.
6. H/O cigarette smoking.
7. Patients with the features of hypothyroidism and obstructive Liver disease.
8. Patients with previous H/o hemodialysis and peritoneal dialysis.

MATERIALS AND METHODS

This study was conducted in Tirunelveli medical college . Patients are selected from all Medical wards. By applying the inclusion and exclusion criteria, we selected 50 patients for our study among them.

A detailed history was taken for the following symptoms suggestive of chronic kidney disease.

- General- Fatigue, Weakness, Pruritus, Bone pain.
- G.I. tract- Anorexia, Nausea, Vomiting.
- Urinary- Nocturia, Polyuria, Oliguria.
- CNS-Numbness, Muscle cramps, Irritability, Hiccough, Seizures and Insomnia.
- CVS- Edema, Difficulty in breathing, Chest pain and Giddiness.

An enquiry for a previous history of diabetes mellitus, hypertension, pulmononary tuberculosis, jaundice, renal disease and drug intake was made.

The patients were examined clinically for the presence of

l.Anemia

2.Edema

3.Hypertension.

4.Pericardial rub.

5.Lung signs.

6.Asterixis and other CNS signs.

7.Abdominal Bruit and ascites and

8.Changes in the Optic fundi:

The following investigations were done

- Urine -Albumin
- Sugar
- Deposits
- Culture sensitivity

Blood- Urea, sugar

Serum- Creatinine, electrolytes.

TC,DC,ESR, HB, Platelet count.

XRay chest PA and abdomen[whenever necessary] Abdominal Abdominal Ultrasonogram: This was done in all cases

Screening for the Ischemic Kidney disease were done with the help of Electrocardiogram and the patients who were all taking the anti ischemic therapy were excluded, because this treatment alters the serum lipid levels.

Similarly Beta blockers - raises the serum LDL level without altering the HDL level.

Thiazide diuretics - raises the triglyceride level and reduce the HDL level.

We took the blood sample for lipid profile analysis in fasting state in patients with Chronic Kidney Disease who fulfills the following criteria.

Fasting lipid profile is taken because eating raises plasma triglycerides, carried mostly in chylomicrons and very low density lipoprotein [VLDL] and as result, total cholesterol levels also increase. The Postprandial increase in cholesterol and triglycerides are variable, depending on the type of food ingested. ln addition, substantial variability in postprandial lipid levels is attributable to inherited and acquired difference between individuals.

Methods used to estimate HDL, Total cholesterol and Triglycerides:

Total Cholesterol- Enzymatic method:

Principle : cholesterol esters converted to cholesterol and fatty acids by cholesterol esterase.

Cholesterol + O_2 $\rightarrow$ choleston-3one +h2o2.

2h2o2+phenolic compound $\rightarrow$ quinonemine.

The intensity of colured complex produced is directly proportional to the concentration of cholesterol content which is measured at 505nm with green filter.

Preparation of working reagent: Dissolve contents of bottle labeled 1 cholesterol with quantity of 2 cholesterol suggested on the bottle label. Mix gently.

Mix standard and sample and incubate for 10mts at 37degree. Read absorbance of standard and test at 505nm.

Test result: interpretated as

Cholesterol concentration = absorbance of test/absorbance of standard ×200.

HDL cholesterol- Immunoinhibition method:

This reagent is intended for in-vitro quantitative determination of HDL cholesterol in human serum.

Reagent named as R1,R2 and R3.

Rl contains goods buffer,4AAP,POD,ascorbate oxidase.

R2 contains Goods buffer, CHE,CO,F-DAOS

R3 contains calibrator

Methodology:

Anti human Beta -lipoprotein antibody in reagent 1 binds to lipoproteins other than HDL. The antigen-antibody complexes formed block enzyme reactions when R2 is added. Cholesterol esterase and cholesterol oxidase in R2 react only with HDL-C. Hydrogen peroxide produced by the enzyme reactions with HDL-C yields a blue coloured complex upon oxidase condenstation with F-DAOS in the presence of peroxidase.The intensity of the blue colour complex formed at 593nm is proportional to the HDL-C in the sample.

Triglyceride Estimation :Enzymatic [GPO/Trinder].

Reagent composition :

Reagent 1 TGL Mono reagent.

LGO611 2×20ml	:	Pipes Buffer
LGO 621 2×50ml	:	4-chlorophenol
LGO 631 5 ×100ml	:	Magnesium ion
		ATP
		Lipase Peroxidase
		Glycerol kinase
		4-aminoantipyrine
		Glycerol-3-po4 oxidase

Reagent 2 TG standard 200mg/dl

LGO 612 l×2.5ml

LGO 622 l×2.5ml

LGO 632 2×2.0ml.

Principle: The estimation of TGL involves the following enzymatic reaction.

Triglyceride +LPL $\rightarrow$ Glycerol +FFA

Glycerol + ATP $\rightarrow$ Glycerol -3-phosphatase +ATP

Glycerol -3 phosphate +02 $\rightarrow$DHAP + h2o.

2H2o2+-DHP $\rightarrow$ Quinoneimine dye + 4h2o.

Absorbance of the quinoneimine dye measured at 505nm is directly proportional to TGL concentrations.

Analysing the sensitivity and specificity of the investigation what we used in this study, We used Plasma urea, serum creatinine, creatinine clearance and USG abdomen were the necessary investigation to satisfy the criteria for the chronic kidney disease.

1) **Creatinine Clearance**:

The staging of chronic kidney disease been done by measuring creatinine clearance for a minute.

The renal clearance of the creatinine is the urine creatinine excretion divided by the area under the plasma creatinine concentration - time curve for the period in which the urine was sampled. The creatinine clearance rate more closely resembles the GFR[20,15].

The reliability is greatly diminished by

1. Variability of the tubular secretion of creatinine .
2. Inability of most patients to collect the urine properly for 24hrs.
3. Prolonged storage of the urine that falsely rise the urine creatinine by 20% [17,19,21].

In order to obviate the well known difficulties in obtaining a complete Urine collection and to have a quick estimate of the GFR when urine can not be, nomograms and formulas have been developed. They

estimate the GFR via the creatinine clearance predicted from the plasma creatinine, body weight, age and gender.

In this study we used **The Cockcroft & Gault [1996] formula** for estimating predicted creatinine clearance for staging CKD patient[29].

Creatinine Clearance for men in ml/mt =[140-Age] × Body wt / S.creat ×72

Age in years

Weight in kgs

Serum creatinine in mg/100ml,for women 85% of the values for men.

2. Equation from the modification of diet in renal disease study[MDRD]. Estimated GFR (mlmin/1.73m^2) = 1.86× (Per) -1.154× (age)-$^{.2O3}$

Multiply by 0.742 for women.

Multiply by 1.21 for African Americans.

Estimated GFR[eGFR] using the CKD- EPI formula:

The CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula was published in May 2009. It was developed in an effort to create a formula more precise than the MDRD formula, especially when actual GFR is >60 ml/min per 1.73 m^2.[18]

Researchers pooled data from multiple studies to develop and validate this new equation. They randomly divided 10 studies which included 8254 participants, into separate data sets for development and internal validation.

16 additional studies, which included 3896 participants, were used for external validation.

The CKD-EPI equation performed better than the MDRD (Modification of Diet in Renal Disease Study) equation, especially at higher GFR, with less bias and greater accuracy. When looking at NHANES (National Health and Nutrition Examination Survey) data, the median estimated GFR was 94.5 ml/min per 1.73 m^2 vs. 85.0 ml/min per 1.73 m^2, and the prevalence of chronic kidney disease was 11.5% versus 13.1%.

The CKD-EPI equation, expressed as a single equation, is:

GFR = 141 X min(Scr/K,l)α X max(Scr/K, l)-1.209 X 0.993Age X 1.018 [if female] X 1.159 [if black][17]

Where Scr is serum creatinine (mg/dl), K is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/ic or 1, and max indicates the maximum of Scr/K or 1.

This formula was developed by Levey et al.

Estimated GFR[eGFR] using the Mayo quadratic formula :

Another estimation tool to calculate GFR is the Mayo Quadratic formula. This formula was developed by Rule et in an attempt to better estimate GFR in patients with preserved kidney function. It is well recognized that the MDRD formula tends to underestimate GFR in patients with preserved kidney function[15,20].

The other formulas & nomograms in use are

1 Edward & Whyte (1959) formula

Creatinine Clearance for men in ml/mt /1.73m^2 = 94.3/sr.creat - 1.8 For women - 85% of the value for men.

2. Jellifes formula 'A'(1971)

Creat Clearance for men in ml/mt/1.73m2 = 100/sr.creat -12. For women = 80/sr.creat -7.

3. Jellifes formula'B'(1973)

Creatinine Clearance for men in ml/mt/1.73m2= [98-16(age-20)/20/sr.creat.

4. Hull (1981) formula.

Creatinine clearance for men in ml/mt/70kg = 145-age(yrs)/sr.ceat.-3.

For women = 0.85(145-Age in yrs)/Sr.creat(mg/dl)[28].

The formula of Cockcroft & gault formula was quoted in over 70 publications n 1991 and displayed in the 1991 Canadian compendium of Pharmaceuticals and specialties as the method of estimating renal functions[21].

There are enough published studies in the last 20yrs to reach meaningful conclusion about the accuracy of predicting the glomerular

functions from the serum creatinine using Cockcroft and gault formula[17,29].

Waller et al in 1991 suggested that the predicted creatinine clearance provides a simpler alternatives to the measured clearance for determining the GFR.[25]

Advantages :

- Timed urine collection is avoided
- Results are available instantly.
- Cost is reduced to less than half of that of the measured Creat clearance[29].

Limitations and possible source of error in this methods :

Age : In children the influence of sex on muscle mass is less important. The concentration in serum may rise but the creat clearance adjusted to the body surface area may remain unchanged.

Body Morphology :

Difference between the predicted and the measured creatinine clearance clearance are seen in very obese , pregnant women and in those with marked muscle wasting.

Lack of stable renal function :

It means that renal function should not have changed greatly over the last 4 days. Unstable renal functions is the most frequent problem in the critical ill, hospitalized patients.

Creatinine assay:

Drugs like salicylate, cotrimoxazole and cimetidine can inhibit tubular secretion of creatinine and thereby increase the serum creatinine concentration without a change in the glomerular function.Ingestion of cooked meat and sternuous exercise may increase the serum creatinine concentration[22,23].

Creatinine secretion:

The mean ratio of the clearance of Tc-DTPA to the measured creatinine clearance was used 1:24 and was 1:13 with the predicted creatinine clearance was 13ml/mt for the measured creatinine clearance and 4ml/mt for the predicted method very little than the regular 24hrs measured method[18].

1) Plasma Urea :

Plasma urea is poor measure of the GFR . Urea production is variable largely depends on the protein intake. Thus the kidneys excrete most of the urea. It can be readily reabsorbed in the tubules .In conditions like low antidiuretic harmone levels, the medullary collecting tubules are

impermeable to urea.In conditions with low effective intravascular volume having high ADH level, the urea reabsorption can be substantial[14].

Substances interfering with the urea estimation- falsely high level are aminosalicylic acid level, bilurubin,lipemia,dextran,uric acid ,free hemoglobin[12,13].

Falsely low level are Vit C, levodopa and lipids .

Serum Creatinine:

It is very insensitive to even substantial decline in GFR. GFR measured by most accurate technique may be reduced upto 50% before serum creatinine becomes elevated. It is insensitive because

1. Sr. Creat with muscle mass

Serum Creat value in young &normal individual indicated The normal GFR. The same level in the elderly individual could indicate a twofold reduction in GFR.

2. Proportional tubular secretion of serum creatinine increases with the decreasing GFR.
3. With the declining kidney function extra renal degradation of the creatinine increases[18].

Methods used to measure Serum creatinine:

- Original folin-wu method- using jaffe reaction
- Method of Hare- using Lloyd reagent
- The direct Alkaline Pictrate method.
- **Auto analyzer using Jaffes reaction[25,20].**

A number of normal plasma constituents can interfere with creatinine measurement. They are glucose, pyruvate, acetoacetate, uric acid, ascorbic acid and plasma proteins. These normal constituents cause Jaffes calorimetric assay to yield high value. These interfering chromogens increase the creatinine value by about 20% [23,24].

One study has shown that in normal individuals the contributions of the nonchromogens in serum creatinine is about 14% and in CKD patient non chromogen contribution in creatinine is about 5 %.[19]

Several modifications in Jaffes reaction have done to remove the interfering chromogens. Fuller earth and ion exchange resins used to remove the non- chromogens.

These methods are replaced by the costlier and convenient auto analyzer technique. These technique perpetuates the creatinine from nonchromogens. In our study we utilized the Auto analyzer method[26].

Ultrasonogram abdomen :

The Ultrasonogram features considered evident of chronic renal failure were

1.Small contracted kidney as evidenced by kidney size equal or less than 9 cm.

2.Poor corticomedullary differentiation.

3.Increased echogenicity based upon which the renal parenchymal disease was graded as follows

Grade 0- normal.

Grade 1- Echogenicity of the renal cortex equal to that of the liver.

Grade 2- Echogenicity of the renal cortex more than that of the liver, but less than that of the renal sinus fat.

Grade 3- Echogenicity of the renal cortex approaching that of the renal sinus fat.

Statistical Analysis :

The Study Subjects were described in terms of percentages and mean values according to their sex and age. The other required analysis and inter group variability were made by the respective test of significance with the usage of the statistical package S.P.S.S. (13.0) at 57 level of significance (p=0.05)

- Ethical committee approval obtained.

BACKGROUND OF THE STUDY

In Tirunelveli Medical College, Lipid analysis is done in fasting state mainly for patients having risk of poor cardiovascular outcome.

Experimental and clinical studies have suggested a correlation between the progression of renal disease and dyslipidemia. High Plasma cholesterol, LDL and Triglyceride level and low HDL level have been demonstrated to be independent risk factors for progression of renal disease from CKD stages 1-5 in humans.

We conducted this study to evaluate the lipid abnormalities in various stages of chronic kidney disease on the background of these references.

We used Cock-Croft & Gault (1976) formula to calculate the predicted creatinine clearance which is a rough estimation of G.F.R. in staging of Kidney disease.

REVIEW OF LITERATURE

CHRONIC KIDNEY DISEASE

Introduction :

The prevalence of chronic kidney disease (CKD) in India is estimated at 7572 per million and end stage Kidney disease at 757per million population, with a staggering financial and social burden. To reduce this burden and improve patient outcome ,Chronic Kidney disease should be detected and treated before the onset of kidney failure through investigation and prompt treatment of CKD[3].

Definition of the chronic kidney disease:

A. Kidney damage for 3 months or longer, as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate manifest by either

1. Pathological abnormalities,
2. Markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in the imaging studies.

B. Glomerular filtration rate less than 60ml per minute per 1.73 m^2 for 3 months or longer with or with out kidney damage[9].

The Prevalence of chronic kidney disease has increased by 16% from the previous decade. The increasing incidence of diabetes mellitus, Hypertension (high blood pressure), obesity and aging population have led to this increase in kidney disease.

Chronic kidney disease is when one suffers from gradual and usually permanent loss of kidney function over time. This happens gradually over time, usually months to years.

Kidney failure occurs when the kidneys partly or completely lose their ability to carry out normal functions[5].

This is dangerous because water, waste, and toxic substances build up that normally are removed from the body by the kidneys.

It also causes other problems such as anemia, high blood pressure, acidosis (excessive acidity of body fluids), disorders of cholesterol and fatty acids, and bone disease in the body by impairing hormone production by the kidneys[44].

CAUSES OF CHRONIC KIDNEY DISEASE

Major causes :

Type 1 and Type 2 Diabetes Mellitus

Hypertension.[1]

Other causes :

- Glomerulonephritis
- Lupus nephritis - Post infectious
- Polycystic Kidney Disease.
- Tubulo Interstitial Nephropathy
- Reflux nephropathy
- Hemolytic uremic syndrome/TTP
- Vasculitis-Wegeners granulomatosis, Polyarteritis nodosa.
- Analgesic nephropathy.
- Ischemic nephropathy[atherosclerosis]
- Obstructive uropathy[5]

Rare causes :

HIV infection, Sickle cell disease, heroin abuse, kidney stones, amyloidosis and cancer.

Risk Factors For CKD:

- Ethnicity
- Gender - male > female

- Smoking
- Heavy consumption of the non- narcotic analgesics.
- Family history of CVD.
- Increased renin angiotensinogen activity
- Thrombogenic factors- antiplatelet agent.

Clue to diagnosis of Chronic disease by analyzing History of the patient

l.Review of symptoms :

Symptoms during urination : usually suggests disorders of urinary tract such as Infections, obstructions or stones.

Recent Infections :

Suggests post-infectious glomerulonephritis or HIV associated nephropathy.

Skin rashes or arthritis :

Suggests connective tissue disorder like SLE or cryoglobilunemia.

Risk factors for parenteraly transmitted disease :may suggests HIV , Hep B , Hep C or associated kidney disease.

2.Chronic diseases :

Heart failure , Cirrhosis, or gastroindestinal fluid losses -usualy suggests reduced kidney perfusion.

Diabetes - starts as microalbminuria then clinical proteinuria and Hypertension[31] .

Hypertension - Hypertensive nephrosclerosis characterized by severly elevated blood pressure followed by end organ damage Recent worsening of hypertension in background of diffuse atherosclerosis indicates large vessel disease. Recent onset of severe HT in young females suggests fibromuscular dysplasia[48].

3.Past Medical History :

Findings from Past routine exam – indicates proteinuria or HT during childhood, during pregnancy, schooling.

Past urological evaluation - gives details regarding radiological abnormalities associated with kidney disease.

4. **Family history of Kidney Disease :**

Every generation, equal susceptibility to male and female- indicates autosomal dominant disease like polycystic kidney disease.

Every generation, male susceptibility- indicates sex linked recessive disorder like Alports syndrome.

Less frequent than every generation - indicates autosomal recessive disease like medullary cystic disease or Autosomal recessive Polycystic kidney disease[5].

Types and Examples of Risk factors for chronic Kidney diseases[1].

	Definition	**Examples**
Susceptibility factors	Increase susceptibility to kidney damage	Older age, family history
Initiation factors	Directly initiate kidney damage	DM. High BP, autoimmune disease, systemic infection. UTI, urinary stone, drug toxicity
Progression factors	Cause worsening kidney damage and faster decline in kidney function after initiation of kidney damage .	Higher level of proteinuria; High BP, poor glycemic control in DM, smoking.

STAGES OF CHRONIC KIDNEY DISEASE[10] :

Stage	Description	GFR ml per m2	Prevalence in (%)	Action
-	At increased risk	>60ml(CKD risk factors)	-	CKD risk reduction
1	Kidney damage with normal or increased GFR	>90	5,900,000(3.3)	Diagnosis and treatment: treatment of the comorbid condition. Slowing the progression
2	Kidney damage with slightly decreased GFR	60-89	5.300,000(3)	Estimating the progression
3	Moderately decreased GFR	30-59	7,600,000(4.3)	Evaluating and treating the complication
4	Severely decreased GFR	15-29	400,000(0.2)	Preparation for kidney replacement therapy
5	Kidney failure	< 15	300,000	Kidney replacement.

Prevalence of GFR Categories in Adults

Age Group (yr)

GFR mL/min/1.73 m	20-39	40-59	60-69	570
>90	86.0%	55.7%	38.5%	25.5%
60-89	13.7%	42.7%	53.8%	48.5%
30-59	*a*	1.8%	7.1%	24.6%
15-29	*a*	a	*a*	1.3%
N (millions):	82	55	20	20

GFR estimated from serum creatinine using MDRD Study equation based on age, gender, race and calibration for serum creatinine. Data from NHANES III (1988-1994). N = 15,000. Based on one-time assessment of estimated GFR.

Fewer than 20 cases; data not considered reliable.

KDOQI Guidelines for Normal GFR in various age groups[10]

Normal GFR in Children and Young Adults

Age (Sex)	Mean GFR±SD(mL/min/1.73 m*)
1 week (males and females)	4O.6 ±14.8
2—8 weeks (males and females)	65.8 ±24.8
>8 weeks (males and females)	95.7 ±21.7
2—12 years (males and females)	133O±27.O
13—21 years (males)	14O.O ±3O.O
13—21 years (females)	126.O ±22.0

***Data based on three studies.**

Abbreviation: SD, standard deviation

Clinical situations in which creatinine clearance may be necessary to measure GFR

1. Extremes of age and body size
2. Severe malnutrition or obesity
3. Disease of skeletal muscle.
4. Paraplegia or quadriplegia.
5. Vegetarian diet.
6. Rapidly changing kidney function
7. Prior to dosing drugs with significant toxicity, that are excreted by kidneys.

Lipoprotein Metabolism:

Lipids circulating in Plasma are incorporated into spherical, water soluble particles [lipoproteins]that contain a core of nonpolar lipids [cholesterol, cholesterol ester and triglycerides] surrounded by a monolayer composed of specific proteins, polar lipids and esterified cholesterol and phospholipids[9].

The Protein components of lipoproteins are called apoproteins. Some of these apoproteins, such as apoprotein A-l in HDL, apoprotein B-100 in LDL, and apoprotein B-48 in chylomicrons.

Metabolic function of Plasma Apoproteins:

Apoproteins	Metabolic Role
A-l	Activates LCAT
A-11	Activates hepatic lipase;may inhibit LCAT
A-lV	unknown
B-48	Transport of lipids from the gut as chylomicrons.
B-100	Transport of lipids from the Liver as VLDL and LDL
C-1	Activates LCAT
C-11	Activates Lipoprotein Lipase.
C-lll	May inhibit activation of lipoprotein lipase by apoC-11
D	May be involved in lipid transfer between lipoproteins.
E	Recognised by hepatic apo E receptors and cellular receptors;
Cholesterol Transfer protein	Facilitates the exchange of cholesterol esters and TGL between HDL and VLDL and LDL.

Four enzymes play pivotal role in lipid metabolism:

- Lipoprotein Lipase
- Hepatic triglyceride lipase
- Lecithin-cholesterol acyltransferase
- Cholesteryl ester transfer protein[32,16].

The major action of Lipoprotein lipase is to degrade TGL rich particles in the postprandial state.

Hepatic lipase has 2 major actions : l] hydrolysis of TGL and phospholipids of HDL2.and2]hydrolysis of TGL of VLDL and IDL.

Hepatic lipase catalyzes hydrolysis and removal of the triglyceride content of HDL. Thus hepatic lipase deficiency can potentially contribute to increased HDL, triglyceride content. In fact, as described later (abnormalities of lipoprotein remnants), CRF results in pronounced hepatic lipase deficiency in humans and experimental animals[33,34].

The enzyme LCAT, which is synthesized in the liver, catalyses the formation of cholesterols esters in the plasma by transferring a fatty acyl chain from phospholipids to the hydroxyl group of unesterified cholesterol.

LCAT plays an important role in HDL-mediated cholesterol uptake from the extrahepatic tissues and, as such, serves as a main determinant of HDL maturation and plasma HDL cholesterol level.

Thus LCAT deficiency can potentially account for diminished plasma HDL cholesterol and impaired HDL maturation in CRF. In fact, plasma LCAT activity is consistently diminished in patients with ESRD. This is accompanied by a significant elevation of plasma-free cholesterol and a marked reduction in plasma esterified cholesterol concentration, providing functional evidence for diminished LCAT-dependent cholesterol esterification[33,34].

The specific transfer protein, CETP, facilitate exchange of cholesterol esters and TGL between HDL and VLDL and LDL

CETP mediates transfer of cholesterol ester from HDL to IDL in exchange for triglycerides. Thus a potential increase in plasma CETP can contribute to the CRF-associated reduction in HDL cholesterol ester and elevation of HDL triglycerides. In fact, according to a recent study, more than 34% of hemodialysis-dependent patients were found to have high plasma CETP levels. The mechanism responsible for the reported elevation of CETP in ESRD patients is unknown and requires future investigation. The effect of CRF is amplified by proteinuria, which has been shown to increase synthesis and markedly raise plasma concentration of CETP. Thus plasma CETP is expectedly elevated in patients with heavy proteinuria and mild to severe renal insufficiency[39].

Metabolism of Very Low density Lipoproteins:

The Liver is the main site of VLDL synthesis . VLDL particles transport endogenous TGL from the liver to peripheral tissues. The Intravascular hydrolysis of VLDL, TGL depends on the activity of Lipoprotein Lipase. LDL is the major product of VLDL metabolism in Human plasma. Diet, freefatty acids, plasma concentration of insulin, glucagon, and epinephrine modulate the secretion of VLDL[16]

Friedewald formula to calculate LDL:

The Friedewald formula appears to be the most practical, reliable method for determining LDL cholesterol in clinical practice: LDL = Cholesterol - HDL- (triglycerides ÷ 5), in mg/dl, or LDL = Cholesterol-HDL- (triglycerides÷2.19), in mmol/l[32].

Two recent studies found the Friedewald formula to be reliable in dialysis patients, although other investigators reported that the percentage error for the formula is higher in patients with CKD compared to the general population. No studies have examined the accuracy of the Friedewald formula in transplant recipients, or studies in other CKD patients, eg, those with nephrotic syndrome.

Recent data from a study in the general population suggest that the Friedewald formula may underestimate LDL in patients with low LDL levels. Data from the general population also suggest that the Friedewald formula is not accurate when triglycerides are >400 mg/dl (>4.52 mmol/l). Direct

measurement of LDL with ultra-centrifugation or immunoprecipitation techniques is reasonably accurate when triglycerides are 400-800 mg/dl (4.52-9.03 mmol/l), but there are no reliable techniques for determining LDL when triglycerides are >800 mg/dl (> 9.03 mmol/l). Fasting triglycerides >800 mg/dl (>9.03 mmol/l) generally indicate the presence of hyperchylomicronemia, and the role of hyperchylomicronemia in ACVD is unknown[36].

There are few studies in children, and none included children with CKD. However, in 1 study of children from the general population, calculating LDL using the Friedewald formula was more reliable in correctly classifying patients with high LDL than was the direct measurement.

LDL is the major cholesterol carrying particle present in the plasma. The liver accounts for 70% of the catabolism of LDL and peripheral tissues account for the remaining 30%.The uptake of LDL by receptor mediated endocytosis cholesterol biosynthesis, an enhanced rate of intracellular cholesterol esterifications, and a reduction in the number of High affinity LDL receptors expressed on the cell surface[30].

Metabolism of High density-Lipoprotein: HDL is generated in the liver from the intravascular lipolysis of VLDL particles and chylomicrons. The newly synthesized HDL contains predominantly protein, free cholesterol, and phospholipids. The apoprotein content of individual HDL particles differs. Some HDL particles contain apo A-

1[HDL2] and apo A-11[HDL3]. Some contains only apo A-l. The half life of HDL is for 4-6days. Epidemological studies in the general population documented an inverse relationship between Plasma HDL cholesterol concentration and risk of coronary heart disease[33,16].

Hepatic SRB-1 is the primary pathway for disposal of HDL-borne cholesterol ester and triglycerides. Therefore, potential dysregulation of this protein can impact HDL metabolism. Heavy glomerular proteinuria has been shown to significantly reduce hepatic SRB-1 protein expression in experimental animals. In contrast, CRF per se, without heavy proteinuria, induced by nephrectomy, does not significantly change SRB-1 mRNA or protein abundance in the liver. However, concomitant heavy proteinuria and renal insufficiency may affect SRB-1 expression and hence, HDL-mediated reverse cholesterol transport[16].

HDL-mediated cholesterol uptake from the extrahepatic tissues depends on deesterification of cholesterol esters contained in the intracellular vesicles and the resultant release of free cholesterol. This process is opposed by ACAT, which is the main enzyme for intracellular esterification of cholesterol. Therefore, a relative increase in ACAT activity can potentially limit HDL-mediated cholesterol uptake and, hence, contribute to the reduction in plasma HDL cholesterol and impaired maturation of HDL. Although the effect

of CRF on ACAT expression and activity in the extrahepatic tissues is not known, CRF has been recently shown to markedly raise hepatic ACAT-2 mRNA and protein abundance, as well as total ACAT activity[33,16].

The potential contribution of ACAT to the CRF-induced dysregulation of HDL metabolism was illustrated by a recent study which revealed that pharmacological inhibition of ACAT results in a dramatic shift in plasma cholesterol from apoB-containing lipoproteins to HDL with virtually no change in plasma total cholesterol in CRF animals. Interestingly, the improvement in the lipid profile with an ACAT inhibitor was accompanied by a significantly higher creatinine clearance in the treated than the untreated animals. This phenomenon may be due to amelioration of dyslipidemia and enhanced HDL-mediated reverse cholesterol transport, leading to attenuation of glomerulosclerosis.

Abnormalities of Lipoprotein metabolism in Chronic Kidney disease.

The dyslipidemia found in CKD patients is usually secondary to their renal disease. The family history provide link to genetic component. Some lipid abnormalities are demonstrable in patients with renal disease even when GFR is normal. But **disorders of lipoprotein metabolism increase in frequency and severity as renal insufficiency develops**.

The most frequent constellation of lipid abnormalities in CKD comprises a decrease in HDL- cholesterol, an increase in VLDL andIDL cholesterol, as well as normal LDL- cholesterol [reflects a redistribution of cholesterol from HDL to VLDL and IDL]. The ratios of Total cholesterol /HDL cholesterol and LDL cholesterol /HDL cholesterol are usually increased[16,33] .

The reduced level of HDL reflects reduction of both HDL 2 and HDL 3 subfractions. In CKD, a defect in cholesterol transport, probably due to diminished LCAT activity and increased activity of CETP, have been documented. The recently proposed index of NON HDL cholesterol, reflecting the sum of LDL and VLDL particles appears to be more sensitive and is a superior predictor of cardiovascular risk.

Hypertriglyceridemia is commonly found in CKD and is the result of both increased synthesis of TGL and VLDL apo B-100 apoprotein in the liver and decreased catabolism of VLDL. Increased TGL and VLDL apo B 100 synthesis in the liver were documented in animal experiments and in CKD patients.

Quantitative changes in Plasma Lipid Profile:

1. Moderate elevation of Plasma TGL concentrations.
2. Low plasma HDL-cholesterol concentrations.
3. High Plasma VLDL and IDL- cholesterol
4. Normal or increased LDL cholesterol

The activity of lipoprotein lipase in plasma and in adipose tissue is decreased in animal experiments and in patients with CKD, even when the plasma TGL is normal. The activity of lipoprotein lipase is influenced by apolipoprotein isoforms, apoprotein C -11 activates and apoprotein C-lll inhibits lipoprotein lipase activity. A decreased ratio of apo C-ll and apo C-lll is observed even in early stages of CKD. Reduced activity of lipoprotein lipase explains the disturbed first step in the breakdown of both chylomicrons and of VLDL . Because of reduced activity of hepatic TGL lipase, the clearance of partially metabolised lipoproteins and chylomicrons is disturbed as well[7].

Aporprotein abnormalities in CKD:

The concentrations of apo A-l and apo A-ll are decreased. In hemodialysis patients it has been documented that decreased apo A1 levels are due to an increased rate of catabolism, whereas reduced apo A-ll levels are primarily due to decreased rate of production. These apoprotein abnormalities are more marked in patients with advanced renal insufficiency and in patients with hypertriglyceridemia. **The apo B concentrations are usually normal in early stages of CKD and are minimally elevated, at best in patients with advanced renal insufficiency.** The ratio of apoA-l/C-111 and apo A-l/B are reduced, and the ratio of apoC-lll/apoE is increased. Similar abnormalities of apo B,C-111 and E concentrations can also be found[7,8].

Qualitative Lipoprotein changes in CKD:

Post ribosomal modification of apolipoproteins by oxidation, glycation and carbamylation. Oxidation does not reduce the affinity of oxidized LDL to the scavenger receptors and oxidized LDL uptake by the macrophage scavenger receptor is increased favouring foam cells. Oxidised LDL exhibits additional atherogenic properties including cytotoxicity and stimulation of thrombotic as well as inflammatory events.HDL protects against the oxidation of LDL. In hemodilayis patient the capacity of HDL patients to prevent LDL oxidation is reduced. The acute phase response changes the HDL composition , transforming HDL from an antioxidant to a pro-oxidant lipoprotein. The reported alterations include an increase in apolipoprotein and serum amyloid A and a decrease paraxonase activity and Platelet activating factor. Serum paraxonase activity reduced in patients with CKD.

IDL, an intermediate of VLDL catabolism accumulates in CKD patients. The IDL concentration is a predictor of severity or progression of atherosclerosis.

LDL particles are heterogenous in size and density. No correlation was found between LDL concentration and LDL size. Small dense LDL accumulate even in early stages of CKD, when total plasma cholesterol and TGL concentrations are still normal[47].

Several theories have been proposed regarding the link between small dense LDL and atherogenicity. l] Their decreased affinity to the LDL receptor combined with their clearance with the scavenger receptor. 2]Their increased susceptibility to oxidation and glycation. 3]Their increased transcapillary escape because of smaller particle size[16].

In CKD patients, Clearance of Chylomicrons is severly impaired.lt has been postulated that postprandial persistence of chylomicrons in the circulation causes endothelial damage and promotes atherosclerosis. This abnormality may contribute to hypertriglyceridemia in CKD[5,7].

LP[a] lipoprotein is a plasma lipoprotein , which contains a protein component called apo[a]. In the general population Lp[a] in high concentration associated with increased cardiovascular risk. ln patients with CKD, prospective studies on the influence of plasma Lp[a] concentrations on atherosclerotic complications have yielded conflicting results[9].

Progression of renal disease in relation to dyslipidemia:

Hyperlipidemia can potentially accelerate progression of renal disease by several mechanisms. First, reabsorption of fatty acids, phospholipids, and cholesterol contained in the filtered proteins (albumin and lipoproteins) by tubular epithelial cells can stimulate tubulointerstitial inflammation, foam cell formation, and tissue injury. Second, accumulation of lipoproteins in glomerular

mesangium can promote matrix production and glomerulosclerosis. In this context, native and oxidized lipoproteins, particularly LDL, stimulate production of matrix proteins by cultured mesangial cells and promote generation of proinflammatory cytokines, which can lead to recruitment and activation of circulating and resident macrophages. In addition, impaired HDL-mediated reverse cholesterol transport can further contribute to tissue injury by limiting the unloading of the excess cellular cholesterol and phospholipid burden. In fact, low plasma HDL has been identified as an independent risk factor for progression of renal disease. Moreover, hereditary LCAT deficiency, which is associated with a marked reduction in HDL cholesterol and impaired HDL-mediated reverse cholesterol transport, results in progressive renal disease. It is of note that both chronic renal insufficiency and nephrotic syndrome lead to acquired LCAT deficiency and impaired HDL metabolism. Correction of these abnormalities by ACAT inhibitor administration has been shown to reduce proteinuria and retard progression of renal disease in experimental animals[43,44].

In addition to the animal studies, a number of clinical studies have provided evidence for the potential contribution of dyslipidemia in progression to renal disease. For instance, the Physicians Health Study demonstrated a significant increase in the risk of deterioration

of renal function among individuals with mildly elevated baseline serum creatinine who had elevated serum cholesterol and/or reduced HDL cholesterol concentrations. Similarly, the Modification of Diet in Renal Disease (MDRD) study identified low plasma HDL cholesterol as an independent risk factor for progression of renal disease. Together, these observations have prompted a limited number of clinical trials exploring the effect of lipid-lowering agents in humans with chronic kidney disease (CKD).

Changes in proteinuria, GFR, and treatment of CKD may alter lipoprotein levels. Therefore, it is prudent to evaluate dyslipidemias more often than is recommended in the general population. Lipoprotein levels may change during the first 3 months of hemodialysis, peritoneal dialysis, and kidney transplantation. On the other hand, waiting 3 months to measure the first lipid profile may needlessly delay effective treatment for patients who present with dyslipidemia[35]. For patients whose lipid profile is normal at presentation, it is reasonable to repeat the lipid profile 3 months later, to confirm that the initial values were not low due to malnutrition or systemic disease. During the course of kidney disease treatment, lipid levels may change. Therefore, the Work Group recommends measuring subsequent levels at least annually. Reasons to repeat lipid measurements after 2-3 months include changes in kidney replacement therapy modality, treatment with diet or lipid-

lowering agents, immunosuppressive agents that affect lipids (eg, prednisone, cyclosporine, or sirolimus) or other changes that may affect plasma lipids[39].

Dyslipidemia in adolescents

Young adults (20-40 years old) with Stage 5 CKD have at least a 10-fold higher risk for CVD mortality compared to the general population. There are limited data on ACVD in children with CKD. However, CVD accounts for approximately 23% of deaths in children and adults <30 years old who started treatment for stage 5 CKD as children. Recent data from the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study provide compelling evidence in the general pediatric population, that initial fatty streaks seen in adolescents develop into atheromatous plaques in young adults. Moreover, this atherosclerotic process is believed to be accelerated in uremia, thus putting children with Stage 5 CKD at high risk for developing ACVD. Indeed, studies of arteries from children with Stage 5 CKD have demonstrated early ACVD changes[10].

Dyslipidemia in Acute Medical conditions :

Some acute medical conditions may transiently alter plasma lipid levels . For example, severe infections, surgery and acute myocardial infarction are often associated with lower-than-normal lipid levels. Other conditions, for example acute pancreatitis, may be associated with higher

levels. In general, it is best to wait until acute conditions that may alter lipid levels have resolved before assessing dyslipidemias for possible ACVD risk. It should be noted, however, that the lipid profile is not significantly altered within the first 24 hours after a myocardial infarction, and a lipid profile can be measured during this time[31].

Acute condition	**Total cholesterol**	**LDL**	**HDL**	**Triglycerides**
Myocardial infarction	↓	↓	↓	NC
Stroke	↓	↓	NC	NC
Bacterial sepsis &surgery.	↓	↓	↓	↑
Acute pancreatitis.	↑	NC	NC	↑
Tranplant acute rejection	↓	↓	NC	↓NC
Transplant CMV infection	↓	↓	NC	↓

Abbreviation, LDL-Low density lipoprotein, HDL-High density lipoprotein, NC-No change, CMV- Cytomegalovirus.

Fasting:

Eating raises plasma triglycerides, carried mostly in chylomicrons and very low-density lipoprotein (VLDL), and, as a result, total cholesterol levels also increase. The post-prandial increases in triglycerides and cholesterol are quite variable, depending on the type of food ingested. In addition, substantial variability in postprandial lipid

levels is attributable to inherited and acquired differences between individuals. Although these differences affect the risk for ACVD, the relationship between post-prandial lipid levels and ACVD is not as well established as the relationship between fasting lipid levels and ACVD.[3] Practical considerations may make non-fasting measurements the only alternative for some patients. While fasting lipid profiles are best, it is better to obtain non-fasting lipid profiles than to forgo evaluation altogether. If the lipid profile obtained in a non-fasting patient is normal, then no further assessment is needed at that time. However, an abnormal lipid profile in a non-fasting patient is an indication to obtain a fasting lipid profile[44,49].

Urine protein excretion, especially if >3 g per 24 hours, can also cause or contribute to dyslipidemias. Therefore, CKD patients who still produce urine should have protein excretion measured, if this has not been done recently. In some cases, the underlying cause(s) of the proteinuria can be treated and effectively reversed. In other cases, angiotensin II converting enzyme inhibitors or angiotensin II receptor blockers may help reduce protein excretion, and may thereby improve the lipid profile in some patients. Clinical hypothyroidism can cause dyslipidemia, and even subclinical hypothyroidism may cause mild changes. Some of the signs and symptoms of hypothyroidism may resemble those of uremia, which may make the clinical diagnosis of

hypothyroidism more difficult in patients with CKD. Glucose intolerance can also cause dyslipidemias. Therefore, patients with dyslipidemia and CKD (but without known diabetes) should be assessed with fasting blood glucose and possibly glycosylated hemoglobin. Glycemic control can improve lipid profiles[32].

Causes of Secondary Lipedemia:

Nephrotic syndrome, hypothyroidism ,diabetes ,excessive alcohol ingestion, and chronic liver disease Medications that can cause dyslipidemias include 13-cis-retinoic acid, anticonvulsants, highly active anti-retroviral therapy, beta-blockers, diuretics, androgens/anabolic steroids, oral contraceptives, corticosteroids, cyclosporine, and sirolimus . The assessment of these secondary causes with history, physical examination, and appropriate laboratory testing is recommended for any patient with dyslipidemia, since effective correction of these disorders may improve the lipid profile[10].

Other causes of secondary lipidemia in adolescent and young adults :

Lipodystrophy; Idiopathic hypercalcemia glycogen storage diseases; cystine storage disease; Gaucher disease; Juvenile Tay-Sachs disease; Niemann-Pick Disease; sphingolipidoses; obstructive liver disease such as biliary atresia; biliary cirrhosis; intrahepatic cholestasis; nephrotic syndrome; anorexia nervosa; progeria; systemic lupus erythematosus; Werner syndrome; and Klinefelter syndrome. These

conditions are fortunately rare, and require referral to appropriate tertiary care specialists[5].

Uses of Statins in Early stage of Kidney disease :

Although the pattern of dyslipidemia with low HDL and elevated triglycerides would be a classic indication for fibrates, fibrates have not been popular in the renal community. This is mainly because most fibrates or their active metabolites accumulate in renal failure and occasionally cause rhabdomyolysis. Alternative interventions, such as dietary changes or switching to polyunsaturated fatty acids, carry a considerable risk of malnutrition or are difficult to implement. The nephrologist is thus left with cholesterol-lowering drugs, such as statins or ezetimibe. Potential indications for statins in patients with renal disease might be to assist in the reduction of proteinuria or to reduce the rate of loss of glomerular filtration (progression) apart from the goal to reduce cardiovascular events[37,51].

Meta-analyses of participants with cardiovascular disease in randomized controlled studies with statins who had impaired renal function and/or proteinuria show a modest, though statistically significant reduction in the loss of eGFR with statins (except in patients with diabetic nephropathy or glomerulonephritis) as well as a modest, significant reduction of proteinuria or albuminuria.

More convincing are findings concerning the effect of statins on cardiovascular endpoints in patients with the initial stages of CKD (CKD stage 2 or early CKD stage 3). The effect of statins has been analyzed in several subgroups of patients with elevated serum creatinine who participated in prospective intervention trials on the effect of statins in patients with high cardiovascular risk. *Post hoc* analyses in these subgroups with impaired GFR suggest that the benefit is at least as high, if not higher, in patients with CKD compared with patients without CKD. A similar effect was observed in the subgroup of patients with diabetic kidney disease. Significant benefit with respect to lowering cardiovascular events is seen in patients with CKD (stage 2 and stage 3) based on serum creatinine concentration and eGFR. In the Cholesterol and Recurrent Events (CARE) study, this was restricted to patients with GFR <40 ml/min with or without proteinuria[37].

Use of Statins in Late Stage of Kidney disease :

Currently, there is a complete lack of controlled information on the effects of statin treatment on outcome in patients with advanced CKD (stage 4). In the past, information on use of statins in dialysis patients had also not been uniform. In an observational study, based on U.S. Renal Data System data, Seliger et al found better survival in a small subgroup of statin users *(*n= 362) compared with nonstatin users *(*n = 3354). More recently, in an open prospective randomized study of a small group of

patients (n = 143) followed over 20 mo, Holmberg et al. found that Atorvastatin had no significant effect on primary cardiac endpoint in patients on dialysis whereas an effect was seen in individuals with pre-end-stage renal disease, potentially suggesting that one may be too late when starting statin treatment if the patient is ready for dialysis[51].

The cumulative incidence of primary composite cardiovascular endpoints comprising death from cardiac causes, fatal stroke, nonfatal myocardial infarction, or nonfatal stroke was not significantly lower over an average observation period of 4 yr (relative risk reduction 8%, 0.77 to 1.10, not significant). There was a positive result, however, for the secondary endpoint of all combined cardiovascular events (205 versus 246 cases in Atorvastatin versus placebo-treated patients, relative risk - 0.82, $P = 0.03$). It remains unclear whether these data in diabetic patients can be generalized or extrapolated to nondiabetic patients. This will be clarified by two ongoing trials (a study to evaluate the use of Rosuvastatin in subjects on regular dialysis: an assessment of survival and cardiovascular events [AURORA] and Study of Heart and Renal Protection [SHARP])[38,53].

Even in early stages of CKD, the cardiovascular risk is dramatically increased. In our opinion, the data from post hoc analyses of past statin trials on subcohorts of patients in the early stages of CKD (CKD stage 2 or early CKD stage 3) are sufficiently suggestive to justify

administration of statins. It is our opinion that statins are indicated in these patients based on these above post hoc analyses. It has even been argued that CKD should be considered a coronary heart disease equivalent, although the magnitude of excess cardiovascular risk in early CKD undoubtedly needs further assessment.

OBSERVATIONS & RESULTS

Results:

Evaluation of the study clients:

The study subjects were evaluated according to their demographic, physiological and bio-chemical characteristics related to chronic kidney disease.

Table -1 Percentage distribution of sex wise study subjects according to their age.

Age group (yrs)	Male		Female		Total	
	No	%	No	%	No	%
15 – 29	1	2.0	3	6.0	4	8.0
30 – 44	8	16.0	3	6.0	11	22.0
45 – 59	16	32.0	6	12.0	22	44.0
60 and above	8	16.0	5	10.0	13	26.0
Total	33	66.0	17	34.0	50	100.0

The above table -1 shows that 44% of C.K.D. patients were in the age group between 45-59. Among them the male and female contribution were 22% and 12% respectively. The mean age of the total subsets was 49.8 ± 13.5yrs. The mean ages of male and female subjects were 50.9 + 12 and 47.7 $\pm$ 16.2 years respectively. The observed difference of mean ages between the sexes was not statistically significant ($P>0.05$).

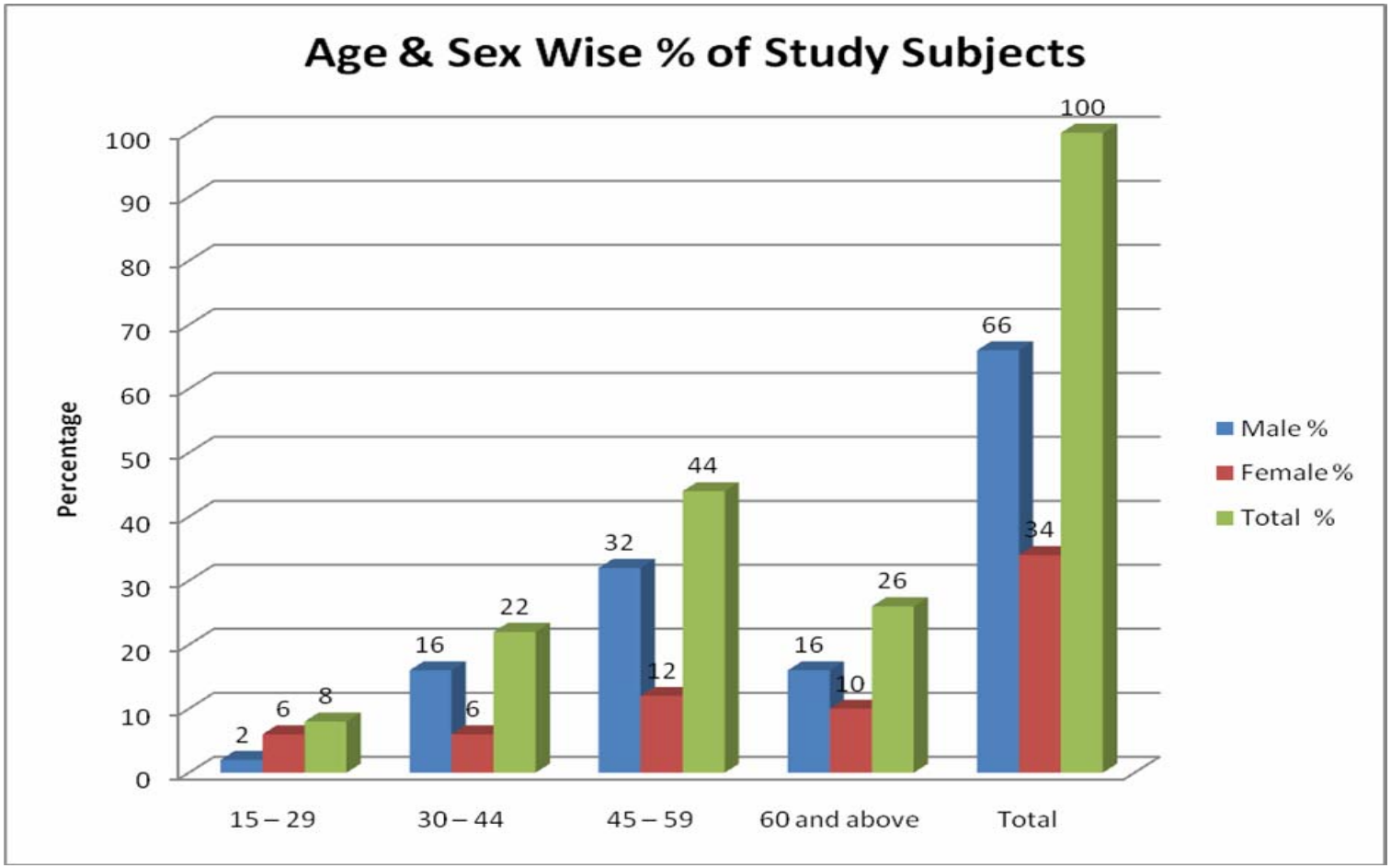

Age & Sex Wise % of Study Subjects
Percentage
100
90
80
70
60
50
40
30
20
10
0
2
6
8
16
6
22
32
12
44
16
10
26
66
34
100
15 – 29
30 – 44
45 – 59
60 and above
Total
Male %
Female %
Total %

Table -2 Sex wise Evaluation of physiological and biochemical characteristics of study participants.

Characteristics	Male			Female			Mean difference	't'	d.f	Signi ficance	Total	
	n	Mean	S.D	n	Mean	S.D					Mean	S.D
Body.wt	33	63.4	6.3	17	55.4	8.4	8.0	3.524	48	P<0.01	60.7	8.5
Bl. Sugar	33	90.5	17.9	17	98.9	19.0	8.4	1.539	48	P>0.05	93.4	18.6
Urea	33	120.3	71.9	17	109.5	48.9	10.7	0.552	48	P>0.05	116.6	64.9
Creatinine	33	6.8	5.6	17	5.8	4.2	1.0	0.606	48	P>0.05	6.5	5.2

d.f. Degree of freedom, S.D – standard deviation

The above table -2 evaluates the study participants according to their body weight, Bl sugar, urea and creatinine. Except body weight, the other variables like Bl. Sugar, urea and creatinine were not significantly different between the sexes (P>0.05). The mean body weights of male and female were 63.4 ± 6.3 kg and 55.4 ± 8.4kg. The difference was statistically highly significant (P<0.01). The total C.K.D. patients mean body weight was 60.7 ± 8.5kgs. The mean Bl. Sugar was 93.4 ± 18.6mg/dl. The mean urea and creatinine were 116.6 ± 64.7 and 6.5 ± 5.2 respectively.

Table -3 Sex wise percentage distribution of hypertensive changes in fundus.

Funds changes	Male		Female		Significance	Total	
	No	%	No	%		No	%
Normal	7	31.8	3	33.3	P>0.05	10	32.3
Grade I	9	40.9	3	33.3	P>0.05	12	38.7
Grade II	6	27.3	3	33.3	P>0.05	9	29.0
Grade III	Nil	-	Nil	-			
Papilledema	Nil	-	Nil	-			
Total	22	100.0	9	100.0		31	100.0

The above table -3 explains the fundus changes of hypertensive patients and found that there was no significant difference was observed between the sexes. Among the hypertensive patients 32.3% was observed as normal. Grade I was 38.7% and Grade II was 29%.

Table -4 Percentage distribution of E.C.G. classification according to their sex.

ECG	Male		Female		Significance	Total	
	No	%	No	%		No	%
Normal	21	63.6	10	58.8	P>0.05	31	62.0
LVH	7	21.2	5	29.4	P>0.05	12	24.0
Hyperakalemia (Tall T waves)	5	15.2	2	11.8	P>0.05	7	14.0
Total	33	100.0	17	100.0		50	100.0

The table -4 illustrates the E.C.G. results of the study subjects and there was no significant difference between the sexes. (P>0.05). The total normal cases were 6.2%. The LVH and hyperkalemic changes were 24% and 14% respectively.

Table -5 Sex wise classification and analysis of creatinine clearance among the study subjects.

Creatinine clearance	Male		Female		Significance	Total	
	No	%	No	%		No	%
<10	12	36.4	6	35.3	P>0.05	18	36.0
10 – 20	4	12.1	6	35.3	P>0.05	10	20.0
20 – 30	8	24.2	4	23.5	P>0.05	12	24.0
30 – 40	9	27.3	1	5.9	P<0.05	10	20.0
40 and above	Nil	-	Nil	Nil	-	Nil	Nil
Total	33	100.0	17	100.0	-	50	100.0

From the evaluation of creatinine clearance shown in the table -5 explains that there was no significant difference between the sexes in respect of level of creatinine clearance except the 4^{th} category (30 – 40) Among the male patients 12 (36.4%) were having creatinine clearance <10 as maximum. Among the female in each category of <10 and 10 -20 were having 6 (35.3%) as maximum. The male mean creatinine clearance was 19.5 ± 11.2 and the same of the female was 15.5 ± 8.9. The difference of mean between the sexes was not statistically significant ($t = 1.296$, $d.f = 48$ and $P>0.05$). The total mean of clearance of total 50 patients was 18.1 ± 10.5.

Table -6 Sex wise percentage distribution of staging of kidney diseases.

Stages of Kidney disease	Male		Female		Significance	Total	
	No	%	No	%		No	%
Stage – III	9	27.3	1	5.8	P<0.05	10	20.0
Stage – IV	11	33.3	8	47.1	P>0.05	19	38.0
Stage - V	13	39.4	8	47.1	P>0.05	21	42.0
Total	33	100.0	17	100.0		50	100.0

The above table -6 shows the stages of sex wise relation of C.K.D. patients. Since there were no study group belong to stage I and stage II they were not included in the table. Among the stage III cases the males (27.3%) were greater than the females significantly (P<0.05). But in the other two stages the sex differences were not statistically significant (P>0.05). Among the total cases, the stage V was greater than other 2 stages.

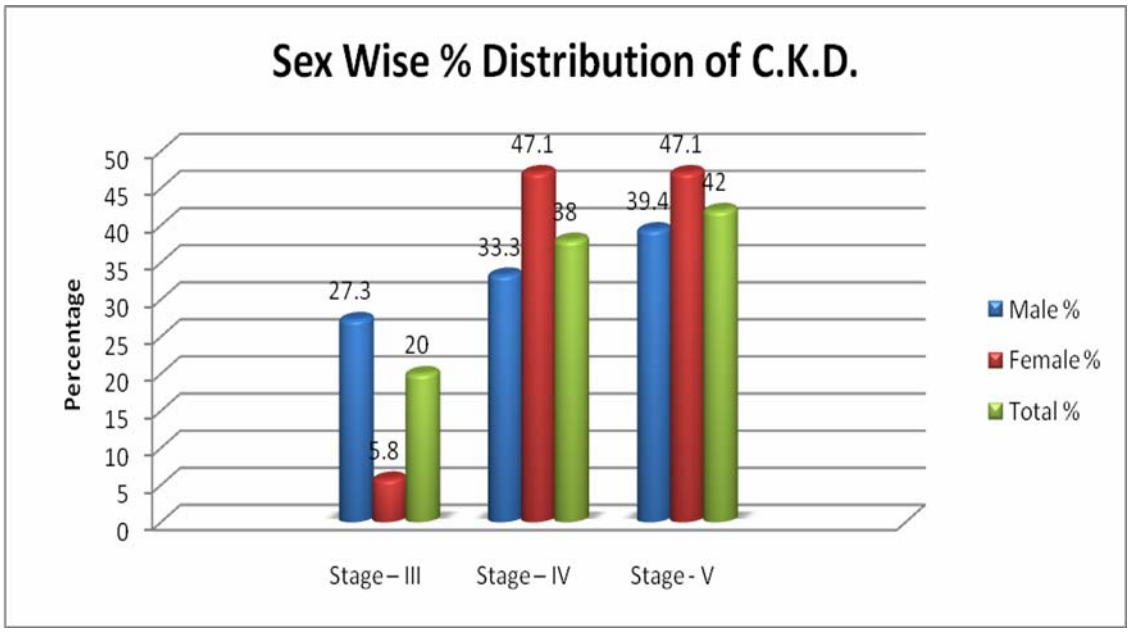


Table – 7 Percentage distribution of lipid abnormalities in the serum sex wise distribution.

Category	Male n=33		Female n=17		Significance	Total n=50	
	No	%	No	%		No	%
Raise in TGL	12	36.4	6	35.3	P>0.05	18	36.0
Raise in LDL	18	54.5	8	47.1	P>0.05	26	52.0
Raise in T.Chl	5	15.2	4	23.5	P>0.05	9	18.0
Decrease in HDL	22	66.7	13	76.5	P>0.05	35	70.0

The above lipid abnormalities among the sex variable of C.K.D were furnished in the above table -7. The results of the above analysis reveal that there was no significant elevation among the sexes were noticed in all lipid elevation namely TGL, LDL and T. cholerterol. The decrease of HDL among the sexes were also not significant. Among the total cases 36% have elevated TGL, 34% have elevated LDL and 18% have T.Cholesterol. In respect of decrease in HDL among the total cases was 70%.

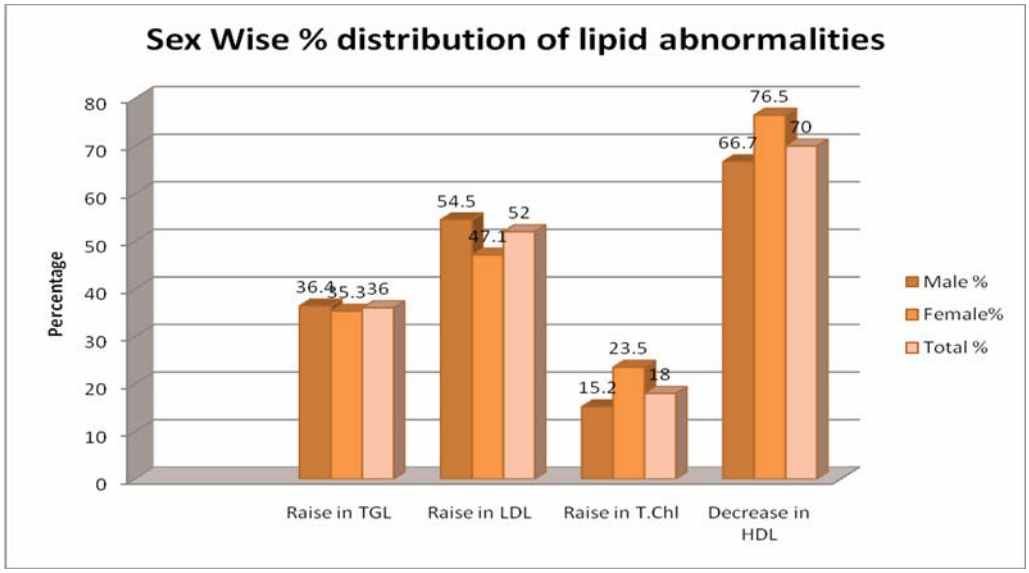


Table -8 Stage wise and sex wise elevated TGL classification of study subjects.

Stages	Male		Female		Significance	Total	
	No	%	No	%		No	%
III	2	16.7	0	0	-	2	20.0
IV	4	33.3	3	50.0	P>0.05	7	38.0
V	6	50.0	3	50.0	-	9	42.0
Total	12	100.0	16	100.0	-	18	100.0

The stage wise and sex wise relation of elevated TGL showed in the table -8 reveals that there was no significant elevation was observed between the sexes (P>0.05) in all stages. The percentage elevated TGL is greatest in stage V group in the study.

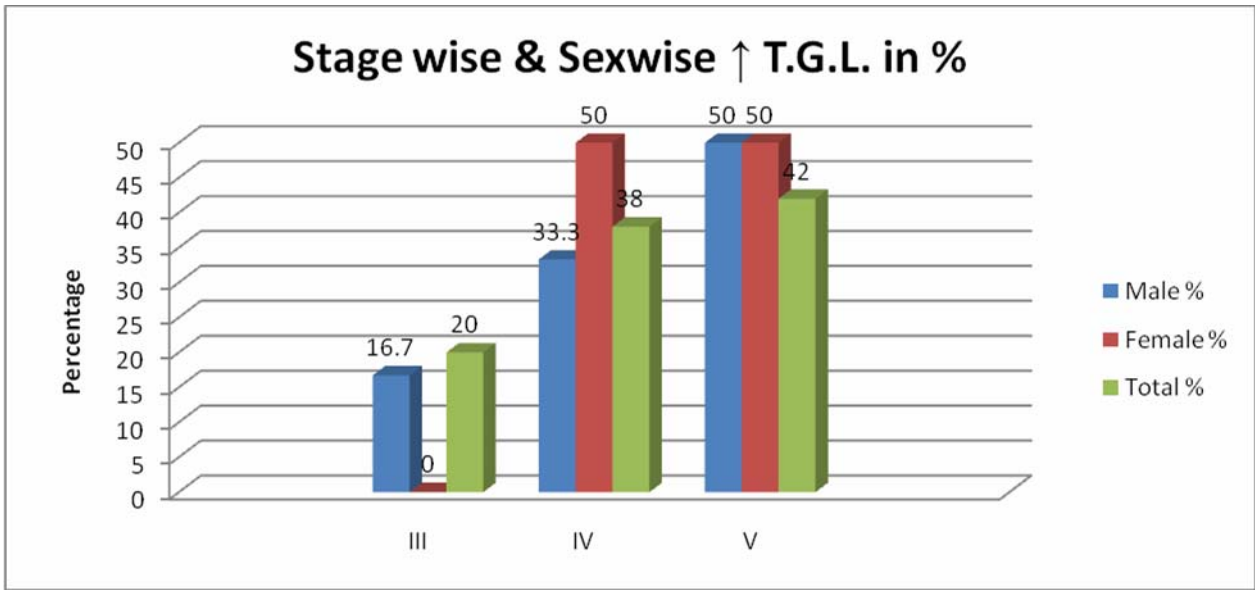


Table – 9 stage wise and sex wise elevated L.D.L. among the study subjects.

Stages	Male		Female		Significance	Total	
	No	%	No	%		No	%
III	4	22.2	0	0	-	4	15.4
IV	4	22.2	4	50.0	P>0.05	8	30.8
V	10	55.6	4	50.0	P>0.05	14	53.8
Total	18	100.0	8	100.0	-	26	100.0

The above table -9 evaluates the elevated level of LDL among the study subjects and according to their sex. The elevated level of LDL between male and female was not significant (P>0.05) in all stages. The percentage elevation in LDL is greatest in stage V CKD than other groups.

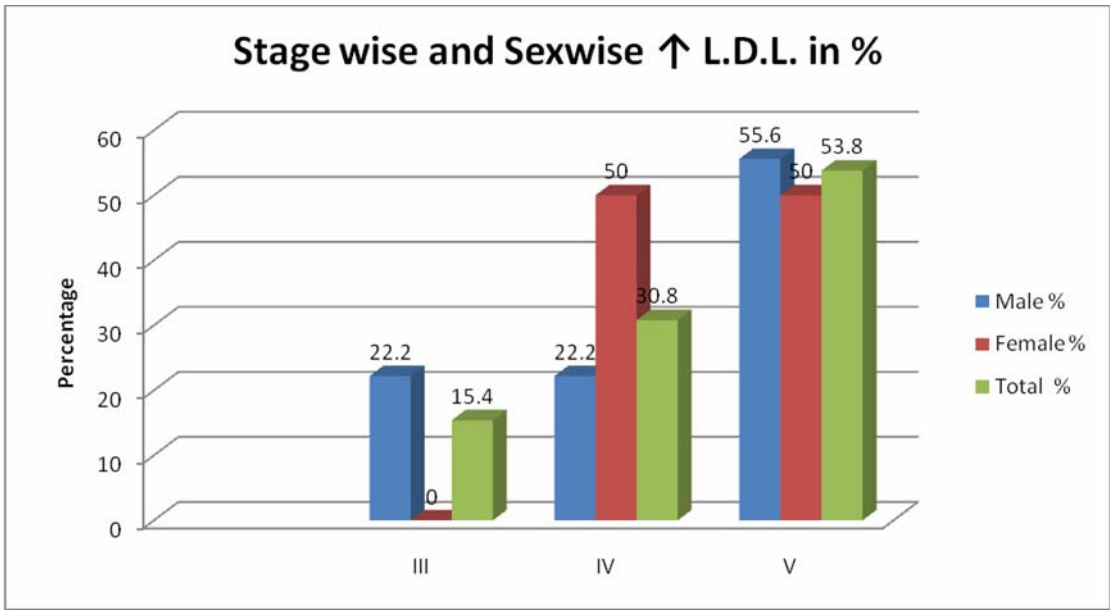


Table -10 Decreased level HDL among the study subjects according to their sex and stage.

Stages	Male		Female		Significance	Total	
	No	%	No	%		No	%
III	5	22.7	1	7.7	P>0.05	6	17.1
IV	8	36.4	7	53.8	P>0.05	15	42.9
V	9	40.9	5	38.5	P>0.05	14	40.0
Total	22	100.0	13	100.0	-	35	100.0

The above, table -10 reveals the decreased level of HDL among the study in relation to male and females sex and found they are of statistically not significant (P>0.05). Further the percentage decrease in HDL is greatest in stage IV CKD when compared to other stages.

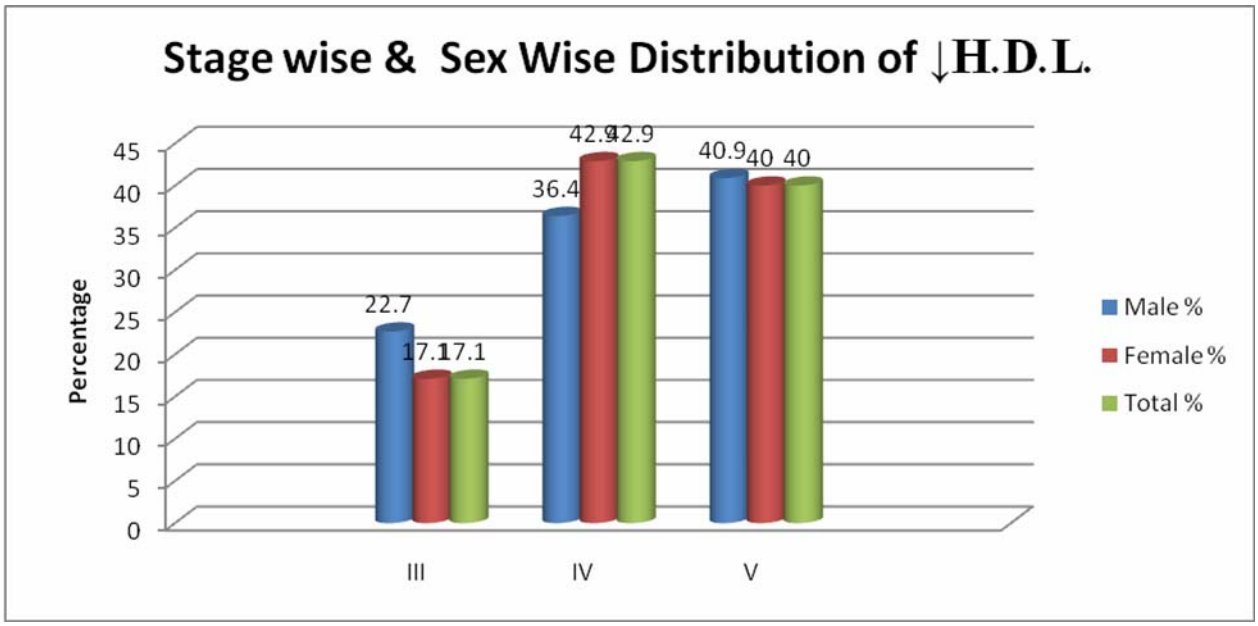


Table-11 Analysis and assessment of sex wise and stage wise LDL level in CKD cases.

Stage	Male			Female			Mean difference	't'	d.f	Signi ficance	Total	
	n	Mean	S.D	n	Mean	S.D					Mean	S.D
III	9	100.6	37.1	1	59.0	0.0	41.6	3.363	8	P<0.01	96.4	37.4
IV	11	103.7	56.4	8	124.6	54.8	20.9	0.806	17	P>0.05	112.5	55.2
V	13	118.3	31.9	8	106.9	49.8	11.4	0.643	19	P>0.05	114.0	38.9
Total	33	108.6	42.2	17	112.4	51.7	3.8	0.280	48	P>0.05	109.9	45.2

The analysis shown in the above table -11 reveals that the mean LDL levels of male and female in IIIrd stage were 100.6 ± 37.1 and 59+0 respectively. The difference was statistically highly significant (P<0.01). In other 2 stages the mean LDL values of male and female were statistically not significant (P>0.05). The total mean LDL of male was 108.6 ± 42.2 and the same of the female was 112.4 ± 51.7. The total LDL levels of both sexes were also not statistically significant (P>0.05).

Table -12 Analysis and assessment of TGL in stage wise and sex wise.

Stage	Male			Female			Mean difference	't'	d.f	Signi ficance	Total	
	n	Mean	S.D	n	Mean	S.D					Mean	S.D
III	9	133.2	62.1	1	102.0	0.0	31.2	1.507	8	P<0.01	130.1	59.4
IV	11	141.0	55.3	8	148.8	67.2	7.8	0.278	17	P>0.05	144.3	58.9
V	13	162.4	69.4	8	129.5	40.7	32.9	1.212	19	P>0.05	149.8	61.1
Total	33	147.3	62.4	17	136.9	53.6	10.4	0.583	48	P>0.05	143.8	59.2

From the analysis of TGL level among the CKD patients shown in the above table -12 states that the mean TGL levels between the two sexes in III stage were 133.2 ± 62.1 and 102.0 ± 0.0 respectively. The difference was not statistically significant (P>0.05). Similarly, the other 2 stages namely IV and V stages, the mean TGL levels between the sexes were not statistically significant (P>0.05).

The total TGL levels of the male was 147.3 ± 62.4 and the total female mean was 136.9 ± 53.6. The difference between the 2 sexes in respect of TGL was not statistically significant. The grand total mean TGL was 143.8 ± 59.2.

Table -13 Analyses and assessment of HDL level among the C.K.D. cases sex wise and stage wise.

Stage	Male			Female			Mean difference	't'	d.f	Signi ficance	Total	
	n	Mean	S.D	n	Mean	S.D					Mean	S.D
III	9	40.2	8.2	1	30.0	0.0	10.2	1.179	8	P>0.01	39.2	8.4
IV	11	36.2	7.5	8	39.1	7.5	2.9	0.832	17	P>0.05	37.4	7.4
V	13	36.0	5.2	8	46.0	9.1	10.0	2.922	19	P<0.05	39.8	8.6
Total	33	37.2	7.1	17	41.8	9.0	4.6	1.965	48	P>0.05	38.8	8.0

The above HDL analysis in table -13 explains the mean HDL level between the sexes in stages of creatinine clearance. In respect of IIIrd and IVth stages, there was no significant difference was observed between the two sexes (P>0.05). In respect to V stage, the mean HDL of male was 36.0 ± 5.2 and the same of the female was 46 ± 9.1. The difference was statistically significant (P<0.05) and inferred that the female were having higher level of HDL than the male in the V stage of CKD. The total mean HDL level of male was 37.2 ± 7.1 and female mean level was 41.8 + 9.0. This difference was not statistically significant P>0.05. The grand total mean HDL level of the study subjects was 38.8 ± 8.0.

Table -14 Stage wise comparison of lipid abnormalities.

Lipids	Stage III n=10		Stage IV n=19		Stage V n=21		Anova F	Significant
	Mean	S.D	Mean	S.D	Mean	S.D		
HDL	39.2	8.4	37.4	7.4	39.8	8.6	0.464	P>0.05
TGL	130.1	59.4	144.3	58.9	149.8	61.1	0.369	P>0.05
LDL	96.4	37.4	112.5	55.2	114.0	38.9	0.553	P>0.05

The mean HDL in stage III, IV, V patients are 39.2, 37.4, 39.8 respectively and their S.D. are 8.4, 7.4, 8.6 respectively. The mean TGL in stage III, IV, V patient are 130.1, 144.3, 149.8 respectively and their S.D are 59.4, 58.9, 61.1 respectively. The mean LDL value in stage III, IV, V are 96.4, 112.5, 114.0 respectively and their S.D are 37.4, 55.2 and 38.2. From this table, the HDL, TGL, LDL value in stages III, IV, V of CKD are not statistically significant (P>0.05) in variation. In other word, the inter group variability of various stages of lipid abnormality are not statistically significant.

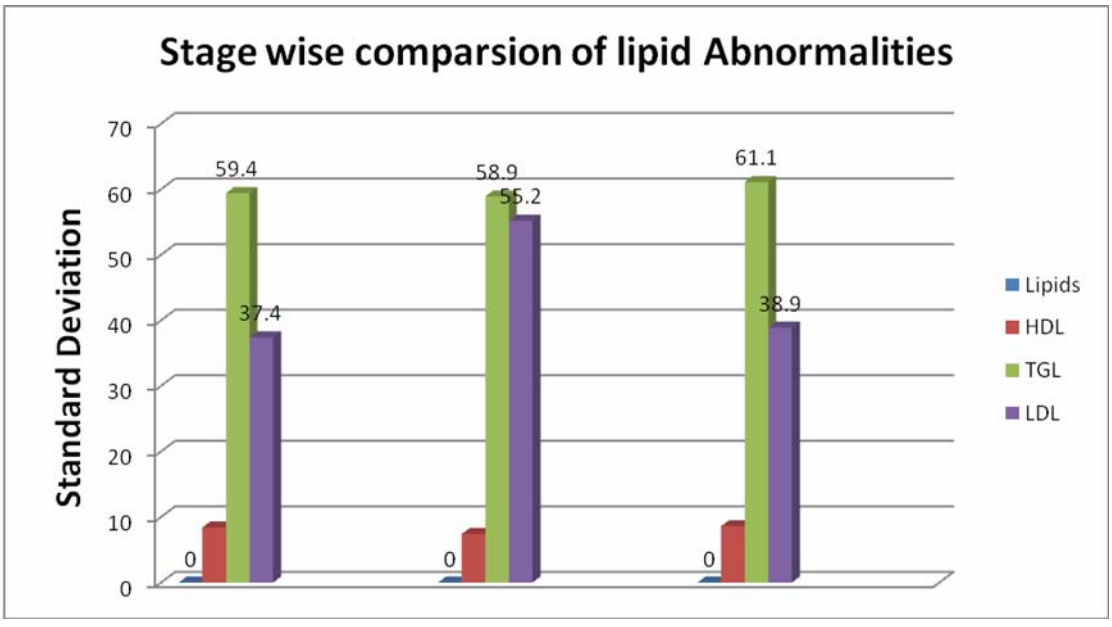
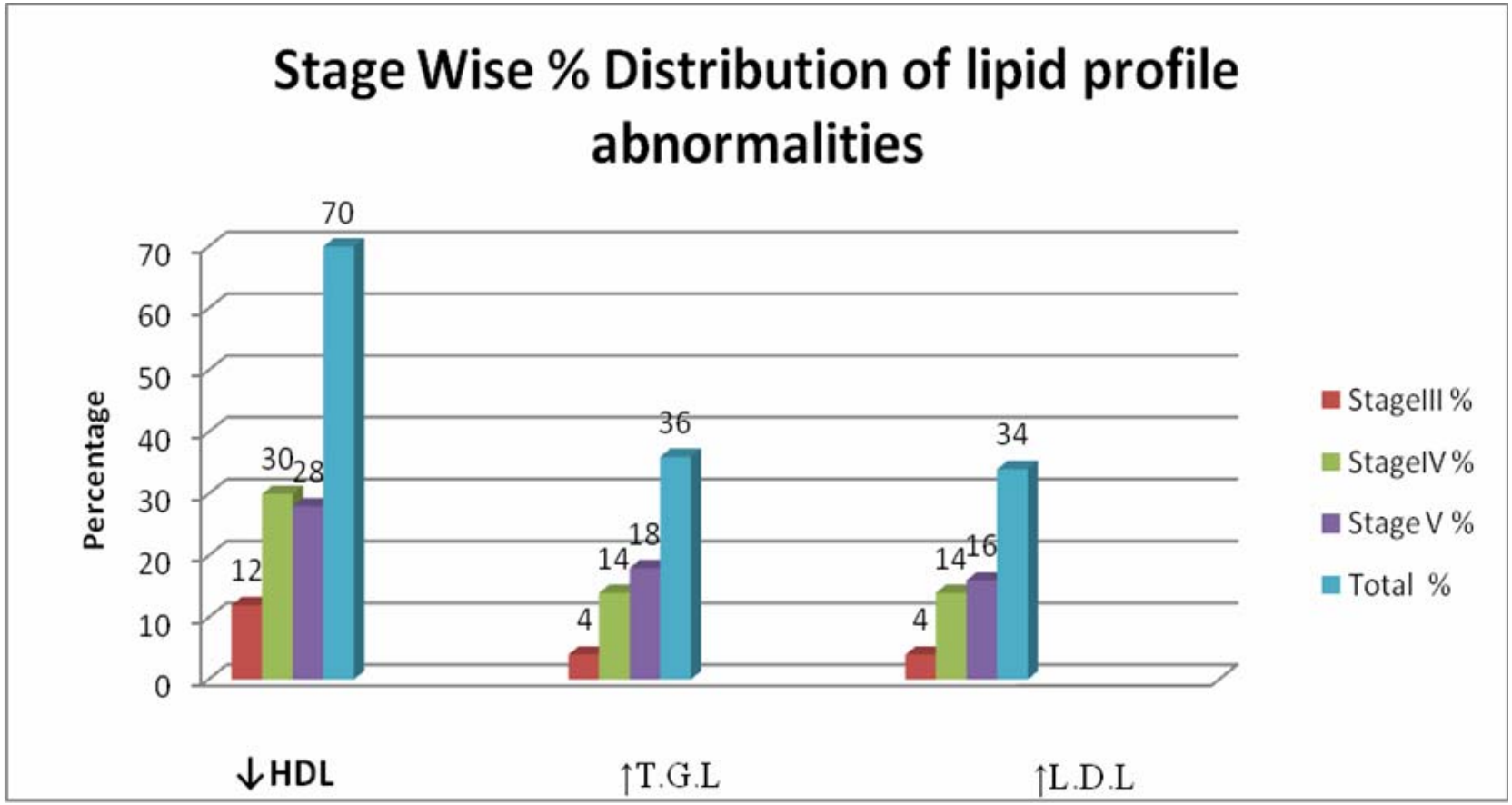


Table -15 Stage wise percentage distribution of alteration in Lipid profile.

Lipid	Stage III		Stage IV		Stage V		Total	
	No	%	No	%	No	%	No	%
↓ HDL n=50	6	12.0	15	30.0	14	28.0	35	70.0
↑ TGL n=50	2	4.0	7	14.0	9	18.0	18	36.0
↑ LDL n=50	2	4.0	7	14.0	8	16.0	17	34.0

The above table shows the stage wise lipid profile alterations. The study group comprising ↓HDL found in 6 (12%) in stage III, 15 (30%) in stage IV, and 14 (28.0%) in stage V CKD. The study group comprising ↑TGL found in 2 (4.0%) in stage III, 7 (14%) in stage IV, 9 (18%) in stage V CKD. The increase in LDL in study group found in 2 (40%) in stage III, 7 (14.0%) in stage IV, 8(16.0%) in stage V CKD. ↓ in HDL was found in 70% of all stages of CKD study group. 36% pts in all stage of CKD study group have increase in TGL. 34% Pts of all stages of CKD study group have increase in LDL. From this study the lipid profile alteration between the stages in term of percentages were statistically not significant (P>0.05).


Stage Wise % Distribution of lipid profile abnormalities
Percentage
70
60
50
40
30
20
10
0
12
30
28
70
4
14
18
36
4
14
16
34
↓HDL
↑T.G.L
↑L.D.L
StageIII %
StageIV %
Stage V %
Total %

DISCUSSION

Risk factors for the atherosclerosis are

1. Central obesity (waist circumference) - >102cms (males) >88cms (females)
2. Hyper Triglyceridemia >150 mg/dl
3. Low HDL <40 mg/dl (males), <50mg/dl (females)
4. Hyper tension >135/85mm Hg
5. Fasting Blood sugar 110 -125 mgs%

The atherogenic – lipid abnormalities in chronic kidney disease patients were elevated LDL, elevated triglycerides and low HDL.

Impaired maturation of HDL in CKD is primarily due to down regulation of lecithin – cholesterol acyltransferase and to a lesser extent, increase plasma cholesteryl ester transfer protein. Trigylceride enrichment of HDL in CKD is due to hepatic lipase deficiency and elevated CETP activity.

The CKD induced Hypertriglyceridemia, abnormal composition, impaired clearance of TGL-rich lipoproteins due to down regulation of lipoprotein lipase, hepatic acyl – COA cholesterol acytransferase.

The apoprotein present predominantly in LDL and TGL are apo B 100. The apoprotein present predominantly in the HDL are apo A-1, which is protective to the atherogenic event.

The apo B48, present predominantly in the chylomicrons are not much atherogenic.

LDL cholesterol – C contains much more apo B 100 level, which is atherogenic, when this LDL is associated with the high TGL level the incidence of atherogenesis is significantly elevated. Multiple lipid abnormalities are more atherogenic.

The study reference was taken from study conducted in Department of Nephrology, University of Medicine, Lublin. They analysed the lipoprotein profiles at various stages of chronic kidney disease. They have done in 502 pts who are not dialysed prior. Their study period was 24mths. According to their study, the significant increase of TG, TC, LDL & ↓ HDL were significantly increased in early stages of kidney disease and in end stage kidney disease there is not much alteration in lipid profile. This is attributed to malnutrition in ESRD in that study.

We have taken the ATP III guidelines and the above standard study as our reference we had undergone the study and analyzed the results.

We had taken the study population from the low socio economic status group. After satisfying the inclusion and exclusion criteria we analysed the lipid abnormalities in all stages of chronic kidney disease, since. We have no study group fits into stage I and II kidney disease, we analyze the other 3 stages of CKD. The decrease in HDL was found to be present in stage III, IV and V stages of CKD amounting to 70% of total. The decrease in HDL observed in 3 group (mean 39.2, 37.4, 39.8) respectively are not statistically significant in severity when compared with stages (P>0.05). Similarly rise in TGL observed in III IV and V stage of CKD having mean value (130.1, 144.3, 149.8) respectively are not statistically significant in severity when compared with stages (P>0.05). The ↑ in TGL in all stages of CKD amounting to 36% total. The rise in LDL obtained in III, IV and V^{th} stages of CKD having mean value (96.4, 112.5, 114.0) respectively, on comparison are not statistically significant (P>0.05). Though we found lipid abnormalities in form of ↑TGL, ↑LDL and ↓HDL in study group in all stage of CKD, This alteration is not statistically significant in severity on comparison by using this statistical package (S.P.S.S) in form of paired 't' test and anova test.

The probable reason offered would be a state of malnutrition in low social economic status group[27]. However large sample size and long duration of study would throw more light upon.

CONCLUSION

The study Dyslipidemia in CKD – Correlation to stages of CKD An evaluation which was conducted in 50 patients in Medical wards of Tirunelveli Medical college Hospital on Non-diabetes kidney disease people has revealed that.

1. The lipid abnormalities are found to occur in all stages of chronic kidney disease.
2. The Reduction in HDL is the most observed lipid abnormality.
3. The lipid abnormalities started to occur even in the earlier stages of chronic kidney disease.
4. However the severity of chronic kidney disease did not correlate with the severity of lipid abnormalities and it was found to be statistically insignificant.

BIBLIOGRAPHY

1. Tsimihodimos V, Dounousi E, Siamopoulos K, C. Dyslipidemia in Chronic Kidney disease. An approach to pathogenesis and treatment. Am J Nephrology 2008;28:958-73.
2. Wu – Wong JR. Endothelial dysfunction and chronic kidney disease. Treatment options. Curr. Opin. Investig Drugs 2008;9(9): 970-82.
3. Weiner DE, Tighiouart H, Amin MG, Stark PC, MacLeod B, Griffith JL, Salem DN, Levey AS, Samak MJ: Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. J Am Soc Nephrol 2004; 15: 1307-1315.
4. Vaziri ND, Moradi H: Mechanisms of Dyslipidemia of chronic renal failure Hemodial Int 2006;10:1-7.
5. Vaziri ND: Dyslipidemia of Chronic renal failure: the nature, mechanisms, and potential consequences. Am J Physiol Renal Physiol 2006;290: F262 – F272.
6. Prinsen BH, de Sain-van der Velden MG, de Koning EJ, Koomans HA, Berger R, Rabelink T.J: Hypertriglyceridemia in patients with chronic renal failure: possible mechanisms. Kidney Int suppl 2003;84:S121-S121-S124.

7. Vaziri ND, Liang K: Down-regulation of tissue lipoprotein lipase expression in experimental chronic renal failure. Kidney Int 1996;50:1928-1935.
8. Lee DM, Knight –Gibson C, Samuelsson O, Attman PO, Wang CS, Alaupovic P: Lipoprotein particle abnormalities and the impaired lipolysis in renal insufficiency. Kidney Int 2002;61:209-218.
9. Attman PO, Samuelsson O, Alaupovic P: Lipoprotein metabolism and renal failure Am J Kidney Dis 1993; 21:573-592.
10. National kidney foundation: K/DOQI clinical practice guidelines for chronic kidney disease; evaluation, classification and stratification. AM J Kidney dis 2002; 39(suppl 1): s1 –s226.
11. Kes. P. Lipid abnormalities in chronic renal failure, nephritic syndrome and dialysis. Acta Med Croatia. 2001; 55(4-5): 177-186.
12. Moller E, Mc Intosh JF, Van slyke DD; Study of urea excretion. II. Relation between urine volume and the rate of urea excretion by normal adults. J Clin invest 6; 427, 1929.
13. Rickers H, Brochner – Mortensen J, Rodbro P; The diagnostic value of the plasma urea for the assessment of renal function. Scand J Urol Nephrol 12:39, 1978.
14. Chasis H, Smith WH; The excretion of the urea in normal man and in subjects with glomerulonephritis. J Clin Invest 17:347, 1938.

15. Steinitz K, Turkand H, The determination of glomerular filtration by the endogenous creatinine clearance, J Clin invest 18; 285, 1940.

16. Diseases of the Kidney, 6th ED. Schrier RW (ED). Little Brown & Co., 1996, 3 vol.

17. Lubowitz H, Slatopolsky E. Shankel S et al; Glomerular filtration rate; Determination in patients with chronic renal failure, JAMA 199; 252, 1967.

18. Lavender S, Hilton PJ, Jones NJ: The measurement of the glomeruler filtration rate in renal disease. Lancet 2; 1216, 1969.

19. Heymsfield SB, Arteaga C, MC Manus C, et al; Measurement of the muscle mass in humans. Validity of 24-hr urinary creatinine method. AM J Clin Neutr 37;478, 1983.

20. Shanmon JA; The renal excretion of creatinine in man. J Clin Invest, 14, 403, 1935.

21. Shemeseh O, Goolbetz H, Kriss JP, Myers BD, Limitation of creatinine as a filtration marker in glomerulopathic patients. Kidney Int 28;830, 1985.

22. Mitch WE, Coolier VU, Walser M; Creatinine metabolism in renal failure. Clin SCI, 58; 327. 1981.

23. Jones JD, Bumett BC; Creatinine metabolism in humans with decreased renal function. Clin Chem; 20; 1204, 1974.

24. Hankins DA, BABB AL, Uvelli DA, Scribner BH; Creatinine degradation. The kinetics of creatinine removal in patients with chronic renal failure. Int J Artif organs 4; 35.1981.

25. Mitch WE, Walser M; A proposed mechanism of reduced creatinine excretion in severe chronic renal failure.

26. Fabiny DL, Ertinsghausen G; Automated reaction rate method for determination of creatinine with Centritichem, Clin Chem 17; 699, 1971.

27. Lipoprotein profile at different stages of Chronic renel insufficiency. Renal failure I.S.S.N. 0886 – 022 x, 2000, Vol 22, pp 63 to 71 (27 ref).

28. Carie BJ, Golbertz HV, Michaelis AS, Myers bd; Creatinine a inadequate filtration marker in glomeruler diseases. AM J Med 69: 177, 1980.

29. Cockraft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976:16; 31-41. Jones C GM, Kusek JW, et al, serum creatinine level US population. Third national health and nutrition examination survey. AM J Kidney Disease 1998; 32: 992.

30. Remuzzi G, Bertani T, Pathophysiology of progressive nephropathies. N Eng J Med 1998: 1448-1456.

31. Jandeleit-Dahm K, Cao Z, Cox AJ, et al. Role of hyperlipidemia in progressive renal disease: focus on diabetic nephropathy. Kidney Int Suppl. 1999;71:S31-S36.
32. Utkowski B, Chmielewski M. Lipid disturbances in chronic renal failure – pathomechanisms and treatment. Rocz Akad Med Bialymst. 2004:
33. Rutkowski B, Lososowska R, Krol E, et al. (Pathomechanism of hyperlipoproteinemia in chronic renal failure). Pol Merkur Lekarski. 2003; 15: 322-323; discussion 323-325. Polish.
34. Rutkowski B, Szolkiewicz M, Korczynska J, et al. The role of lipogenesis in the development of uremic hyperlipidemia. Am J Kidney Dis. 2003; 41 (3 Suppl 1): S84-S88.
35. Harper CR, Jacobson TA. Managing dyslipidemia in chronic kidney disease. J Am Coll Cardiol, 2008; 51: 2375-2384.
36. Sanfelippo ML, Swenson RS, Reaven GM. Reduction of plasma triglycerides by diet in subjects with chronic renal failure Kidney Int. 1977; 11: 54-61.
37. Trippoli GF, Navaneethan SD, Johnson DW, et al Effects of statins in patients with chronic kidney disease. Meta-analysis and meta-regression of randomized controlled trials. BMJ, 2008; 336: 645-651.

38. Tonelli M, Isles C, Curthan GC, et al. Effect of pravastatin on cardiovascular events in people with chronic kidney disease. Circulation. 2004; 110: 1557-1563.

39. Kwan BC, Kronenberg F, Beddhu S, Cheung AK. Lipoprotein metabolism and lipid management in chronic kidney disease. J Am Soc Nephrol. 2007; 18: 1246-1261.

40. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culeton B, Hamm LL, Mc Cullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P, Pfeffer M, Raji L, Spinosa DJ, Wilson PW: Kidney disease as a risk factor for development of cardiovascular disease a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 2003; 108: 2154 – 2189.

41. Hallan SI, Coresh J, Astor BC, Asberg A, Powe NR, Romundstad S, Hallan HA, Lydersen S, Holmen J: International comparison of the relationship of chronic kidney disease prevalence and ESRD risk J Am Soc Nephrol 2006; 17:2275-2284.

42. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization, N Engl J Med 2004;351:1296 -1305.

43. Riesen WF, Mordasini R: Hyperlipidemia in renal failure: Phenotypes and pathogenic mechanisms. Contri'b Nephrol 41:312-320, 1984.

44. Manaske CL: Lipid abnormalities and renal disease, kidney (Natl Kidney Fndtn) 20:25-30, 1988.

45. Chan MK, Varghese Z, Moorhead JF: Lipid abnormalities in uremia, dialysis, and transplantation. Kidney Int 19:625-637, 1981 PubMed ISI ChemPort.

46. Keane WF, Kasiske BL, O'Donnell MD: Lipids and progressive glomerulosclerosis. Am J Nephrol 8:261-271, 1988 PubMed ISI Chemport.

47. Culleton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. Kidney Int 1999;56:2214.

48. Shulman NB, Ford CE, Hall WD, Blaufox MD, Simon D, Langford HG, et al; The Hypertension Detection and Follow-up Program Co-operative Group. Prognostic value of serum creatinine and effect of treatment of hypertension on renal function. Results from the hypertension detection and follow-up program. Hypertension 1989; 13 (Suppl): 180-193.

49. Keane W.F., (1994): Lipids and Kidney. Kidney Int. 31; 1153-1159.

50. Joven J., Vileela E., Ahmad S., Cheung M.C., Brunzell J.D. (1993): Lipoprotein heterogenecity in end-stage renal disease. Kidney Int. 43: 410-418.
51. Ritz E., Augustein J, Bommer J., Gnasso A., Haberbosh W. (1985): Should hyperlipedemia of renal failure be treated? Kidney Int. Vol. 28, Suppl, 17; S?84-S?87.
52. Cheung, AK, Parker, CJ, Ren, K, Iverius, PH. Increased Lipase Inhibition in uremia: Identification of pre-B-HDL as a major inhibitor in normal and uremic plasma, Kidney Int 1996; 49:1360.
53. Attman PO, Alaupovic P. Lipid abnormalities in chronic renal insufficiency. Kidney Int 1991; 39: S16-S23.
54. Prevalence of chronic kidney disease based on estimated glomerular filtration rate and proteinuria in Icelandic Authors: Viktorsdottir, Olof; Palsson, Runolfur; Andresdottir, Margret B., Aspelund, Thor; Gudnason, Vilmundur; Indridason, Olafur.

PROFORMA

NAME		
AGE		
SEX	IP NO:	
	BASIC DISEASES	
CAHD	HT	DM
EDEMA	OLIGURIA	HEMATURIA
ABD DISTENSION	DYSPNEA	FACIAL PUFFINESS
	G/E	
ANAEMIA	SKIN CHANGES	
BP	NAIL CHANGES	
	INVESTIGATIONS	
SUGAR		
UREA		
SR. CREATININE		
SR. ELECTROLYTES		
SR.SODIUM		
SR.POTASSIUM		
URINE ALBUMIN		
CREATININE CLEARANCE		
CHEST XRAY PA VIEW		
ECG		
USG	KIDNEY SIZE	
	RIGHT	
	LEFT	
SR.LIPID PROFILE		
HDL		
LDL		
VLDL		
TGL		
T.CHOLESTEROL		

MASTER CHART

MASTER CHART CONTAINS THE DATAS FOR THE DYSLIPIDEMIC CHANGES IN PATIENTS WITH C.K.D.

Sl. No.	NAME	AGE	SEX	IP NO	DM	HT	CAHD	WT	BP	SUGAR	UREA	CREAT	URINE ALB
1	PONNUSAMY	52	M	22357	-	3	-	68	150/100	110	120	9.2	Nil
2	PITCHAMMAL	64	F	35105	-	-	-	62	130/70	124	81	3.1	Nil
3	MADASAMY	54	M	35208	-	-	-	66	120/70	90	109	10.2	Nil
4	IBRAHIM MEERAL	62	F	31050	-	4	-	70	140/70	116	119	17	Nil
5	MOOKIAH	54	M	36050	-	6	-	68	140/90	96	280	9.9	Nil
6	VENKATESAN	39	M	36109	-	-	-	60	120/80	92	58	2.2	++
7	KALLIAMMAL	45	F	35159	-	-	-	50	120/80	105	130	6.5	Nil
8	SELVA RAJ	44	M	34422	-	2	-	68	160/110	68	72	3.4	+
9	ROSI	25	F	35086	-	-	-	48	130/170	95	58	2.8	Nil
10	SOLAI MUTHAMML	59	F	36190	-	2	-	52	160/110	92	178	12.6	Nil
11	MUTHURAMALINGAM	40	M	34682	-	2	-	66	140/110	86	66	3.2	+
12	SUBBAMMAL	54	F	32700	-	3	-	56	140/90	102	120	5.5	Nil
13	PERATCHI	62	F	33742	-	8	-	45	140/100	102	72	2.2	Nil
14	SELVI	23	F	33924	-	-	-	46	130/80	70	88	3.4	Nil
15	RAJANANI	40	F	33997	-	-	-	52	140/90	80	116	9.3	Nil
16	LAKSHMANAN	58	M	27771	-	4	-	60	150/110	88	62	3.8	+
17	MUPPIDATHAMMAL	55	F	34325	-	5	-	48	160/100	100	72	2.6	Nil
18	PAULSAMY	40	M	29903	-	4	-	77	140/100	105	168	14.2	Nil
19	KANDASAMY	56	M	29892	-	3	-	45	145/100	79	81	4.4	Nil
20	SUBBULAKSHMI	45	F	42356	-	-	-	62	120/70	106	60	2.6	+
21	MALSAMY	65	M	30921	-	-	-	62	90/60	108	72	2.9	Nil
22	MUPPIDATHI	55	M	24925	-	4	-	54	190/100	89	178	17	Nil
23	ABULJOTHI	33	F	34603	-	1	-	60	110/100	87	189	5.8	Nil
24	MADASAMY	51	M	34870	-	3	-	70	150/110	118	78	2.6	++
25	PARAMASIVAM	61	M	34195	-	4	-	58	140/90	102	333	16	Nil
26	RASOOL MOHAMMED	48	M	22396	-	4	-	70	170/100	62	150	9.2	Nil
27	MARAGATHAMMAL	44	F	22470	-	-	-	66	110/70	96	85	3.6	Nil
28	ARUMUGA RAJA	18	M	36933	-	-	-	46	140/90	50	271	21	Nil
29	SUBRAMANIYAN	65	M	37335	-	-	-	68	120/70	104	160	3.2	Nil
30	SIVANAND	65	M	36923	-	-	-	64	130/80	101	121	4.4	Nil
31	MURUGAN	57	M	44168	-	5	-	62	160/100	106	99	3.3	Nil
32	PANDI	52	M	31922	-	4	-	66	180/100	92	48	2.6	Trece
33	CHELLIAH	65	M	50450	-	-	-	62	110/70	94	88	2.3	+
34	GOMATHI NAYAGAM	57	M	50384	-	4	-	55	110/110	96	82	3.2	Nil
35	CHELLATHAI	64	F	54356	-	6	-	54	140/90	106	198	7.3	Nil
36	ALAGAR	30	M	58476	-	-	-	62	150/100	68	110	5.5	Nil
37	ESAKIMUTHU	40	M	51427	-	-	-	64	1730/70	94	64	2.9	+
38	LEELAVATHI	45	F	16342	-	3	-	66	140/100	146	66	2.8	+
39	JOHN	54	M	53946	-	4	-	68	160/100	112	68	3.1	+
40	KETTIPOMMU	64	F	55226	-	5	-	50	130/100	87	55	2.3	Trece
41	MARIAPPAN	32	M	54523	-	1	-	56	140/104	71	201	14.6	Nil
42	JEGAVEERA PANDIAN	59	M	38285	-	3	-	76	100/100	91	46	2.8	+
43	RAJESWARI	30	M	38006	-	-	-	52	120/70	86	105	19.5	Nil
44	PITCHIAH	68	M	39076	-	-	-	18	140/80	104	209	8.4	Nil
45	DEVARAJ	65	M	36720	-	4	-	66	160/100	65	68	2.8	++
46	SIVANAND	48	M	39326	-	7	-	70	170/100	113	86	3.2	Nil
47	PERIYA KARUPAMY	60	M	40428	-	6	-	68	140/100	60	72	2.3	++
48	AGUSTIN	46	M	38294	-	4	-	64	160/100	75	64	2.6	+
49	PONNUSAMY	52	M	22537	-	5	-	64	150/100	110	120	9.2	Nil
50	PONNAMMAL	17	F	40872	-	-	-	42	130/90	68	177	10	Nil

MASTER CHART

MASTER CHART CONTAINS THE DATAS FOR THE DYSLIPIDEMIC CHANGES IN PATIENTS WITH C.K.D.

Sl.No.	NA +	K +	CR.CLEARANCE	FUNDUS	ECG	USG	ABD	SR. LIPID PROFILE				
						R.K in cms	L.K in cms	HDL	LDL	VLDL	TGL	T.CHOL
1	137	3.6	8.5	Gr II	N	7.8x3.4	8.2x3.6	37	144	23	114	204
2	144	5.1	17.9	N	N	9.0x3.3	8x4.1	39	86	50	250	175
3	140	5.9	7.7	N	TALLT	6.4x3.3	7x4	46	62	29	144	137
4	141	5.5	3.8	Gr II	N	6.8x4.2	7.4x4.4	53	157	34	171	244
5	125	3.7	8.2	Gr I	LVH	8.3x3.6	8.6x2.7	30	124	44	222	110
6	128	3.4	38.3	N	N	7.9x3.3	8.1x3.6	49	110	19	86	176
7	134	4.5	8.6	N	N	6.9x4.19	7.9x3.2	57	95	31	157	177
8	143	5.8	26.7	Gr I	LVH	6.6x4.2	7.5x3.2	28	88	13	65	129
9	54	2.2	33	N	TALLT	6x3	5.6x2.3	30	59	20	102	109
10	126	4.5	3.9	Gr I	LVH	7.7x3.2	8.6x3.4	31	66	19	95	116
11	146	5.6	28.6	Gr I	N	5.6x3.4	7.5x3.2	51	75	30	151	156
12	141	4.2	10.3	N	LVH	9.4x4.2	9x4.2	46	133	27	133	189
13	58	2.4	18.8	Gr II	LVH	8.2x3.6	8.4x4.2	40	56.8	19.8	99	77
14	133	4.9	18.7	N	TALLT	6.9x2.1	7.7x2.8	40	151	15	115	176
15	136	5.4	6.6	Gr II	N	9.2x3.6	9.5x3.4	38	171.2	37.2	186	132
16	122	6	24.4	Gr I	N	6.2x3.6	5.8x3.2	42	77	21	103	98
17	122	4	18.5	Gr II	LVH	3.6x6.3	9.1x7.2	46	80	20	101	46
18	119	4.8	7.2	Gr II	LVH	5.2x2.6	7.6x3.1	30	120	54	269	204
19	143	5.4	11.9	N	LVH	8.2x3.6	8.6x4.2	42	117	14	72	173
20	140	3.8	26.7	N	N	8.6x3.2	8.4x3.6	26	97	30	102	143
21	131.2	4.5	22.3	N	N	7.2x3.6	8.6x3.4	38	53	29	146	120
22	162	5.8	3.8	Gr I	TALLT	6.4x3.6	5.8x3.2	40	85	52	260	177
23	132	4	13.5	N	N	9.8x3.8	8.8x4.2	41	57	27	130	145
24	134.7	3.8	33.3	N	N	6.2x3.4	5.9x3.1	36	89	16	81	141
25	142	6.5	4	N	LVH	5x2.6	7.8x3.1	41	119	37	188	123
26	134.6	4.6	9.7	Gr II	LVH	7.2x3.2	7.0x2.7	33	110	40	250	183
27	129	4.2	20.8	N	N	8.6x4.2	8.8x4.4	50	125	40	199	215
28	137.2	3.7	3.7	N	N	7.4x3.4	7.8x3.4	42	176	46	232	172
29	140	2.5	22.1	N	N	7.5x3	7.8x3.9	44	70	55	274	169
30	140	4.5	15.2	N	N	7.0x2.5	7.0x2.7	33	44	28	142	105
31	131	3.3	21.7	Gr II	N	8.6x4.2	8.8x4.3	34	216.8	36.8	184	214
32	141	5	31	N	LVH	7.7x3.2	6.6x2.7	46	131	20	99	197
33	129	3.8	28.1	N	N	8.8x2.2	8.2x4.6	42	147	27	138	162
34	123	4.6	19.8	Gr II	N	9.2x4.4	9.2x3.8	24	60	20	102	104
35	122	3.7	6.6	N	LVH	8.6x4.2	8.8x4.3	55	38	14	32	107
36	138	4.5	16.9	N	N	8.8x4.2	8.4x3.9	38	176	46	202	174
37	137	3.7	30.7	N	N	9.2x4.2	8.8x3.8	36	168	36	182	168
38	109	3.4	26.4	Gr II	N	8.6x4.2	8.8x4.2	32	200	44	224	188
39	136	5.6	26.2	Gr I	TALLT	8.4x4.2	8.2x2.2	38	134	14	71	186
40	142	4.9	23.4	Gr II	N	8.6x4.6	2.8x4.6	40	201	18	90	259
41	125	5	5.8	N	N	7.8x3.6	6.8x2.7	30	107	16	80	155
42	139	4.5	30.5	N	N	6.9x3.2	6.6x3.9	54	126	20	101	200
43	121	5.5	3.5	N	N	7.6x3.4	6.6x2.7	36	154	24	124	165
44	146	3.7	2.1	N	N	7.7x3.2	6.6x2.7	27	76	19	92	122
45	144	4.3	31.2	N	N	7.7x3.2	6.6x2.7	34	46	27	136	157
46	141	4.7	28	Gr II	TALLT	8.4x4	8.8x4.4	30	70	49	247	149
47	140	5.2	32.9	Gr II	N	9.2x4.2	9.4x4.4	32	99	29	144	103
48	137	6.2	32.1	Gr I	TALLT	7.3x3.6	7.7x3.8	31	75	19	96	125
49	137	3.6	8.5	Gr II	N	8.4x4	8.6x4.6	37	144	23	114	204
50	128	3.5	6.1	N	N	7.6x3.2	6.6x2.6	48	138	18	92	204